Incidence of Hospitalisation for Heart Failure and Case-Fatality Among 3.25 Million People with and without Diabetes

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Incidence of Hospitalisation for Heart Failure and Case-Fatality Among 3.25 Million People with and without Diabetes

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Abstract

Background—Recent clinical trials of new glucose-lowering treatments have drawn attention to the importance of hospitalisation for heart failure as a complication of diabetes. However, the epidemiology is not well described, particularly for type 1 diabetes. We examined the incidence and case-fatality of heart failure hospitalisations in the entire population aged 30 and older resident in Scotland during 2004 to 2013.

Methods—Date and type of diabetes diagnosis were linked to heart failure hospitalisations and deaths using the national Scottish registers. Incidence rates and case-fatality were estimated in regression models (quasi-Poisson and logistic regression respectively). All estimates are adjusted for age, sex, socio-economic status and calendar-year.

Results—Over the 10-year period of the study, among 3.25 million people there were 91,429, 22,959 and 1,313 incident heart failure events among those without diabetes, with type 2, and type 1 diabetes respectively. The crude incidence rates of heart failure hospitalisation were therefore 2.4, 12.4 and 5.6 per 1000 person-years for these three groups. Heart failure hospitalisation incidence was higher in people with diabetes, regardless of type, than in people without. Relative differences were smallest for older men, in whom the difference was nonetheless large (men aged 80, rate ratio 1.78; 95% CI 1.45 to 2.19). Rates declined similarly, by 0.2% per calendar-year, in people with type 2 diabetes and without diabetes. Rates fell faster, however, in those with type 1 diabetes (2.2% per calendar-year, RR for type 1/calendar-year interaction 0.978; 95% CI 0.959 to 0.998).30-day case-fatality was similar among people with type 2 diabetes and without diabetes, but was higher in type 1 diabetes for men (OR 0.96; 95% CI 0.95 to 0.96) and women (OR 0.98; 95% CI 0.97 to 0.98). Case-fatality declined over time for all groups (3.3% per calendar-year, OR per calendar-year 0.967; 95% CI 0.961 to 0.973).

Conclusions—Despite falling incidence, particularly in type 1 diabetes, heart failure remains around 2-fold higher than in people without diabetes, with higher case-fatality in those with type 1 diabetes. These findings support the view that heart failure is an under-recognised and important complication in diabetes, particularly for type 1 disease.

Key Words: Epidemiology; Electronic Health Records; Registries; Diabetes Mellitus; Type 1; Diabetes Mellitus; Type 2; Incidence; mortality.

Clinical Perspective

What is new

- Heart failure incidence has fallen over time for people with and without diabetes, but is around 2 times higher in people with diabetes than people without diabetes
- Heart failure case-fatality is higher in people with type 1 diabetes
- Duration of diabetes and glycated haemoglobin was associated with increased risk of heart failure in type 1 and type 2 diabetes

What are the clinical implications?

- Clinicians should be aware of the importance of heart failure in diabetes, especially in type 1 diabetes, where this risk is under-appreciated

Introduction

Recent clinical trials of new glucose-lowering treatments have drawn attention to the importance of hospitalisation for heart failure as a complication of diabetes.[1–4] However, little is known about the epidemiology of heart failure in unselected individuals with type 2 diabetes, and even less about those with type 1 diabetes.

We have examined the incidence of heart failure for an entire country, and how this has changed over time. All residents in Scotland receive care from the National Health Service which is free at the point of contact. All diabetes-related community (primary care) and hospital outpatient encounters in Scotland are recorded in a centrally-accessible database and these are linked to national hospitalisation and mortality records. Given the prognostic import of developing heart failure, we have also investigated the case-fatality related to incident heart failure hospitalisation and how this has changed over time.

Specifically, we examined the incidence rate for heart failure hospitalisation and 30-day case-fatality following heart failure hospitalisation over a 10-year period from January 2004 to December 2013 among people with diabetes (type 1 and type 2).

Methods

Access to data and methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure. However, individual-level data are available via application to NHS Information Services Scotland,[5] aggregate data are provided in the supplementary appendix (Supplemental Tables 1 and 2), and analysis code has been posted online.[6]

Datasets

We used data from the population-based Scottish diabetes register linked to national hospitalisation and death records. The Scottish diabetes register is derived from primary and secondary care records for people with diabetes diagnosed in normal clinical practice using blood glucose measurements and/or HbA1c with coverage of >99% since 2004,[7] the start of the study period. Anyone alive in Scotland aged 30 and older at any time from 2004 to 2013 was included in the analyses.

Definition of heart failure

Heart failure was identified from the first mention in any position (primary or secondary diagnoses) in hospital in-patient records using codes from the ninth (ICD-9) and tenth (ICD-10) International Classification of Diseases revisions (402, 402, 402.1, 402.2, 402.4, 402.6, 402.9, 425.5, 428, 428, 428.1, 428.9 and I11.0, I13.0, I13.2, I42.6, I50.0, I50.1, I50.9 respectively). Outpatient attendances with heart failure are not recorded in the Scottish national healthcare database, nor in the Scottish diabetes register.

Diabetes status and diagnosis date

Date and type of diabetes were obtained from the diabetes register based on the clinician-recorded date of diagnosis. Diabetes status was defined as type 2 diabetes, type 1 diabetes and no diabetes.

Covariates

Age at first heart failure hospitalisation and sex were identified from hospital admission and mortality records. Socio-economic status was assessed via an area-based measure of deprivation which is assigned to residents of Scotland on the basis of where they live using the Scottish Index of Multiple Deprivation (SIMD).[8] SIMD 2009 combines 31 indicators across seven

domains: income—employment, health, education, housing, geographic access, and crime. The index is generated from a weighted sum of the seven domain scores for each area defined by postcodes (zip codes) which contain a median of 769 people. SIMD data were missing for approximately 1% of hospital admissions or death records and these records were excluded from the analysis.

Clinical risk factors

As an additional analysis, in order to explore the association between demographic and clinical risk factors and subsequent risk of heart failure admissions, we also identified a closed cohort from the Scottish Diabetes Register. All patients in this cohort had been diagnosed with type 1 or type 2 diabetes on or prior to the 1st of October 2013 and had not had a heart failure admission in the 10-years prior to this date. Follow-up data was available for three years.

Heart failure in the closed cohort was defined as per the main analysis. However, the clinician-recorded diabetes type was corrected through the use of additional clinical information (eg medication use) as described in a previous publication.[9]

For this cohort, baseline characteristics such as glycated haemoglobin, body mass index, duration of diabetes, blood pressure, and retinopathy were also obtained from the diabetes register, taking the mean (or mode) of all measures not more than 3-years prior to the start date. Data on current prescriptions for selected drug classes (Supplemental Table 3) was also obtained, as was data on previous stroke and myocardial infarction within the previous ten years.

Statistical analysis

Hospitalisations and deaths

Using the population-based Scottish diabetes register, linked to national hospitalisation and death records, heart failure hospitalisations from January 1st 2004 (or the date at which each person

was diagnosed with diabetes, if this occurred during the study period) to December 31st 2013 were identified for people with diabetes aged 20-89 years. Heart failure hospitalisations were defined as incident if these were the first to occur on or after January 2004 where no previous heart failure hospitalisation had been recorded during the preceding 10-years (Supplemental Figure 1). As with our previous analyses we used a fixed period to define incident cases to avoid bias from non-observation of prevalent cases.[10] This analysis was replicated using the entire national hospitalisation and death record to identify heart failure hospitalisations for the general adult population. Incident hospitalisations were summed by calendar-year, age, sex, deprivation decile and, for the diabetes dataset, diabetes type. Within the levels of these stratifying variables, the number of incident heart failure hospitalisations in people without diabetes was derived by subtracting the diabetes heart failure hospitalisations from the general population heart failure hospitalisations.

Case-fatality was examined at 30-days, defined as the proportion of patients who died from any cause within 30 days of any heart failure hospitalisation. Both in-hospital and out of hospital deaths were included.

Person-time

As for hospitalisations, person-time for people with diabetes was estimated using the linked diabetes register, hospitalisation and death data. Each individual's person-time was estimated as the number of days from the start of the study period (or date at which each person was diagnosed with diabetes, if this occurred during the study period) to the date of the incident heart failure hospitalisation, death or censoring at December 31st, 2013 (Supplemental Tables 4 and 5). This was summed by diabetes type, calendar-year, age, sex, and deprivation decile. Mid-year population estimates for the general population in Scotland, stratified by age, sex and deprivation

were obtained from National Records of Scotland. For people without diabetes, person-time not at risk (due to prevalent or incident heart failure events) was also summed by the same stratifying variables. Within the levels of these stratifying variables, person-time for people with no diabetes was obtained by subtracting the diabetes person-time from the mid-year estimates population estimates.

Modelling

Heart failure incidence rates were estimated by age, sex, deprivation, calendar-year and diabetes status. Confidence intervals for the rate ratios and rate differences were obtained as per Rothman.[11]

For the main analysis, regression models were fit using non-parametric smooth terms (penalized thin plate regression splines) and interaction terms to allow for non-linearity and heterogeneity respectively. We used regression in preference to stratification to avoid categorising continuous variables, which can result in unstable estimates if a stratum is too small, and loss of information if a stratum is too heterogeneous.

Interactions are reported on the same scale as the main effects as the RR or OR, since this can be interpreted as the relative difference in the magnitude of an association per one-unit change in the interacting variable.

For incidence rates, generalized linear models were used with a log-link and Poisson error distribution, using a scaling factor (quasi-Poisson) to allow for overdispersion. Age in years was divided by ten so that each increment was a decade (eg age 44 was transformed to 4.4). Deprivation deciles were treated as a deprivation score ranging from 1 to 10, which was divided by 5 such that each increment was a 5-point increment. Terms were included for main effects in all models regardless of significance or magnitude of effect. The large and heterogeneous study

population with a large number of events allowed us to investigate whether the magnitude of risk associated with diabetes varied by biologically plausible and clinically relevant variables on the basis of prior knowledge of diabetes and heart failure. Interaction terms (between 2 or more of age, sex, deprivation and diabetes status) were retained if the exponentiated coefficient (on the transformed scale) was ≥ 1.05 or ≤ 0.95. However, for interactions with calendar-year, all statistically significant interactions (at $P < 0.05$) were included in the final models. Using the same covariates, generalized linear models with a logit-link and binomial error distribution were used to model both heart failure prevalence and case-fatality.

In additional analyses these models were repeated after excluding patients with a previous admission for ischaemic heart disease (ICD-9 410-414 or ICD-10 I20-25), and in separate sensitivity analyses after adding additional ICD-10 codes (I42.0, I42.7, I42.8, I42.9) for cardiomyopathy, and after restricting the analysis to admissions where heart failure was the primary diagnosis (recorded in the first of six possible diagnostic positions).

For the analysis of the association between the 3-year risk (odds) of heart failure and clinical and demographic characteristics in the closed cohort, we used logistic regression models. Covariate missingness was addressed using multiple imputation (supplementary appendix). We fitted models for type 1 and type 2 diabetes, and a third model which included covariate/diabetes-type interaction terms to compare risk factor associations between type 1 and type 2 diabetes. Multiple imputation was used for missing data (Supplemental Table 6).

The association between heart failure and drug prescription was not modelled due to the high likelihood of confounding by indication. However, we did compare the odds of cardiovascular medication prescription in people with type 2 versus type 1 diabetes. Each drug class was modelled unadjusted, adjusting for age and sex, and for the risk of heart failure (on the

logit scale) according to each person's baseline characteristics. The latter was derived from the model of 3-year risk in the closed cohort described above.

SPSS was used to extract the administrative data and R version 3.4.3 (Vienna, Austria) was used for the statistical analyses.

Approval for the creation and analysis of the linked dataset containing no person-identifying information was obtained from the Scottish Care Information - Diabetes Collaboration (SCI-DC) steering committee, the Scottish multi-centre research ethics committee (reference number 11/AL/0225), the Privacy Advisory Committee of NHS National Services Scotland and Caldicott guardians.

Results

This study included the entire Scottish population who were aged 30 or older at any time between 2004 to 2013. In 2004, this comprised 3,066,253 people without a diagnosis of diabetes, 136,042 with a diagnosis of type 2 diabetes and 18,240 with a diagnosis of type 1 diabetes. Of these 1,642,022 (53.6%), 63,086 (46.4%) and 8,141 (44.6%), respectively, were women and the mean (and standard deviation [SD]) ages were 52.9 (15.3), 65.0 (12.2) and 50.0 (14.1) years, respectively. SIMD was similar across the groups with mean (SD) deprivation scores of 5.5 (2.9), 5.9 (2.8) and 5.6 (2.8), respectively.

Incidence of heart failure hospitalisation

28,681 people without diabetes, 3,480 with type 2 diabetes, and 382 with type 1 diabetes were excluded because of a previous heart failure hospitalisation (Supplemental Figures 2 and 3, Supplemental Table 7). Over the 10-year period of the study, among the 3.25 million people remaining there was 91,429, 22,959 and 1,313 incident heart failure events (during 38,112,739.9,

1,855,281.8 and 235,924.2 person-years) among those without diabetes, with type 2 diabetes, and with type 1 diabetes, respectively.

Heart failure incident hospitalisation estimated rates from Poisson regression models adjusting for age, sex and deprivation are shown in Figure 1 (and additionally in Supplemental Figures 4 and 5 and in Supplemental Table 8). For illustration, age-sex stratified rates for 2013 are shown in Table 1. Rates varied markedly with age and differed according to sex and whether or not diabetes was present.

Overall, the rate of incident heart failure hospitalisation rose steeply with age, was somewhat higher in men than in women and was higher in individuals with diabetes than in those without this diagnosis. Incident heart failure hospitalization was also higher in people with type 1 compared to type 2 diabetes.

We found the *relative* risk of diabetes-related heart failure hospitalization (as indicated by the rate ratio) was highest in younger people and higher in women than men (Figure 1 and Table 1). However, as the absolute rate of incident heart failure was highest in older individuals, the greatest difference in absolute rates were also seen in these groups, and not in younger people and women (Figure 1).

Time trends in incident heart failure hospitalisation

Across the period studied, the rate of incident heart failure hospitalisation fell slightly, at around 0.2% per calendar-year (RR per calendar-year 0.998; 95% CI 0.991 to 1.005).

In models adjusting for age, sex and deprivation, the rate of decline was slightly steeper in older individuals. The rate of decline was 0.5% per calendar-year faster per ten-year increment in age (RR for interaction 0.995; 95% CI 0.992 to 0.998), and was similar in men and women

(RR for interaction 1.006; 95% CI 0.998 to 1.014), and according to deprivation (RR for interaction (per 5-point increment in deprivation score) 0.996; 95% CI 0.989 to 1.003)

From the same model, trends in heart failure incidence rates in people with type 2 diabetes were similar to those in individuals without diabetes over a ten-year period from 2004 (Figure 2, Supplemental Tables 9 and 10). However, there was some evidence of a more rapid decline in people with type 1 diabetes, where the decrease was 2.2% per calendar-year faster than in people without diabetes.

An interactive version of Figure 2, where diabetes type and sex-specific temporal trends can be shown for patients of any age or with any level of socio-economic deprivation, is available at https://ihwph-hehta.shinyapps.io/dm_hf_fig2/.

Notwithstanding any temporal decrease in absolute rates, the rate ratios for heart failure hospitalization remained large throughout the study period for both types of diabetes. For example, in 2013 the rate ratios in people with type 2 diabetes, compared to those with no diabetes, were 5.81 (95% CI 4.91 to 6.86) and 3.55 (95% CI 2.99 to 4.21) for 50-year-old women and men, respectively.

Case-fatality of incident heart failure hospitalisation

Over the period of the study, 14.2% (16406/115701) of people admitted to hospital with heart failure died within 30-days of admission.

30-day case-fatality results obtained from logistic regression models adjusting for age, sex and deprivation are shown in Figure 3 (see supplementary appendix for model coefficients, including interactions). For illustration, age-sex stratified case-fatality is shown in Table 2. Case-fatality varied markedly with age and differed according to sex and whether or not type 1 diabetes was present. It was higher in women than in men and in older people than in younger

people. However, it was similar in people with type 2 diabetes and in people without diabetes, for men the odds ratio (OR) was 0.96 (95% CI 0.95 to 0.96) and for women the OR was 0.98 (95% CI 0.97 to 0.98).

However, case-fatality was higher among people with type 1 diabetes compared to people without diabetes; the difference was larger for men (OR 1.91; 95% CI 1.68 to 2.18) than for women (OR 1.31; 95% CI 1.05 to 1.65).

Trends in case-fatality were also modelled adjusting for age, sex, deprivation, calendar-year and type of diabetes (Figure 4, Supplemental Tables 11 and 12). The rate of decline was around 3.3% per calendar-year (OR per calendar-year 0.967; 95% CI 0.961 to 0.974) in people without diabetes. There was no evidence of a steeper decline in people with type 1 diabetes (OR for calendar-year/type 2 interaction 1.011; 95% CI 0.959 to 1.065) or type 2 diabetes (OR for calendar-year/type 2 interaction 0.994; 95% CI 0.979 to 1.009.)

Incidence of heart failure hospitalisation without previous ischaemic heart disease

Incident heart failure hospitalisation was lower in people who had never had a previous admission for ischaemic heart disease admission (ICD-9 410-414 or ICD-10 I20-25), with rates per 1,000 person-years (py) of 1.7 (65,657 events/38,117,663.1 py), 9.2 (17,175 events/ 1,867,390.1 py) and 3.6 (841 events/ 236,843.7 py) for the no-diabetes, type 2 diabetes and type 1 diabetes groups respectively. Nevertheless, the rate ratios for both type 1 and type 2 diabetes in this group (Figures 5, Supplemental Figures 6 and 7, and Supplemental Tables 13-16) were similar to those in the whole cohort (Figure 1).

Risk factors for heart failure in people with diabetes

28,8208 people with type 2 diabetes and 26,189 with type 1 had not had a previous hospital admission with heart failure on October 1st 2013. In this cohort, over 3-years of follow-up the risk of heart failure was 6752 (2.3%) and 231 (0.9%) for type 2 and type 1 diabetes respectively. Age, sex, body mass index, estimated glomerular filtration rate, smoking, previous ischaemic heart disease and stroke all predicted an increased risk of heart failure, although no associations were found for systolic blood pressure, total cholesterol or HDL cholesterol (Table 3). After adjusting for conventional risk factors, longer duration of diabetes and higher concentrations of HbA1c also predicted heart failure risk. Of note, there was no evidence that any of the predictors of heart failure differed between type 1 and type 2 diabetes.

People with type 2 diabetes were more likely than those with type 1 diabetes to have a current prescription for a range of cardiovascular drugs (Table 4). Across all drug-classes examined, compared to people with type 1 diabetes, those with type 2 diabetes were more likely to have been prescribed cardiovascular medications. For loop diuretics and antiplatelets the risk was not higher after adjusting for age and sex (OR 0.87; 95% CI 0.82-0.93 and OR 1.03; 95% CI 0.99-1.07 respectively. However, for the remaining cardiovascular drug classes (including lipid lowering drugs, drugs acting on the renin-angiotensin system and calcium channel blockers) higher prescription levels in type 2 diabetes persisted on adjusting for age and sex, and on adjusting for the predicted risk of heart failure (Table 4).

Sensitivity analyses

On restricting incident heart failure admissions to those where heart failure was the primary diagnosis, the heart failure incidence rates were around half of those reported for any incident admission, with rates per 1,000 person-years (py) of 0.9 (34,893 events/38,080,361.9 py), 6.1

(11,551 events/ 1,885,715.8 py) and 2.7 (635 events/ 237,683.5 py) for the no-diabetes, type 2 diabetes and type 1 diabetes groups respectively. Nonetheless, compared to the main analysis (Figure 1, Supplemental Figures 4 and 5 and Supplemental Table 7) similar associations were found (Supplemental Figures 8 and 9 and Supplemental Tables 17-19). On adding cardiomyopathy codes (I42.0, I42.7, I42.8, I42.9) to the heart failure definition used in the main analysis, similar results were also found; this was true for the absolute incident rates and case-fatality, and the rate ratios and odds ratio comparing the three groups (type 1, type 2 and no diabetes).

On comparing the clinician-recorded and *corrected* clinician-recorded definitions of diabetes type in the closed cohort, similar associations between type of diabetes and 3-year risk of heart failure were found; adjusting for age, sex and deprivation, the odds ratios were 1.24 (95% CI 1.09-1.40) and OR 1.21 (95% CI 1.05-1.38) respectively.

Discussion

We documented the rate of incident heart failure hospitalisations in a large and complete national dataset which included over 250,000 people with diabetes among a population of more than 3.25 million people aged ≥30 years, in whom there were more than 115,000 first hospitalisations for heart failure.

We examined trends in these rates, and the associated 30-day case-fatality, over a ten-year period (2004-2013). Importantly, we reported these rates and trends separately for people with type 1 as and type 2 diabetes.

We found that the age and sex adjusted rates of incident heart failure hospitalisation were around 2-fold higher in people with diabetes, regardless of type, compared to those without

diabetes. In all groups, there was a decline in incidence rate of around 2% over the decade studied, with a slightly greater rate of decline in people with type 1 diabetes than in the other groups studied.

In terms of trends, heart failure incident hospitalisation appears to be falling more quickly over time (both in absolute and proportional terms) in people with type 1 diabetes, compared to people with type 2 diabetes and to people without diabetes. The difference was moderate; having adjusted for age, sex and deprivation the decline was faster in those with type 1 diabetes (2.1% per year versus 0.2% per year). We are not aware that this finding has been reported previously, but it is consistent with an observation from the Swedish registry that the rate ratio for type 1 diabetes and incident heart failure was larger in the 1998 to 2004 period than in the 2005 to 2011 period.[2]

We also found that the relative difference in heart failure incidence between people without diabetes and those with type 1 or type 2 diabetes was larger for younger people and for women than for older people and men. This is consistent with previous reports.[1–3] It is important to note, however, that because of the higher overall rates in men and older people, the absolute differences in heart failure incidence were larger in these groups. Therefore, from the perspective of the individual patient, the impact of diabetes on heart failure risk is greater at older ages and in men. Indeed, the absolute difference in one-year risk of heart failure admission in 80-year old men (the group with the smallest relative difference) with and without diabetes was 2.5%. For the same comparison, but in 40-year old women, the difference was less than 0.5%.

Unlike incidence, for case-fatality the relationship with diabetes depended on the type of diabetes. Case-fatality was similar among people with type 2 diabetes compared those without

diabetes. However, among people with type 1 diabetes, case-fatality was 1.3-fold higher in women, and 1.9-fold higher in men.

Women therefore have a 2-fold higher heart failure incidence and a 1.3-fold higher case-fatality. In combination, this means that compared to women without diabetes, women with type 1 diabetes have around a 2.5-fold higher risk of having an incident heart failure admission which results in death within 30-days. For the equivalent comparison in men, there is almost a 4-fold difference in risk.

Elevated incidence rates for heart failure admission among people with type 2 diabetes have been reported previously. One study using the Clinical Practice Research Database (CPRD) used primary care records to define heart failure and type 2 diabetes. The authors identified 34,198 people with type 2 diabetes from 1998 to 2010. Among women over the age of 60 with and without type 2 diabetes, they found a relative difference (hazard ratio) of 1.50.[3] We obtained a similar relative difference (rate ratio) of 2.12 (95% CI 2.06-2.17). For men over 60, the comparable figures were 1.43 and 1.93 (95% CI 1.88-1.98) respectively. The fact that we included only hospitalisations, and not primary care attendances, may account for the slightly stronger associations we report.

In the international REACH registry, there was also an elevated risk of heart failure hospitalisation among the 19,699 people with diabetes (type unspecified) compared to people without diabetes.[1] However, the magnitude of the association in this cohort, which mainly included people with established atherothrombotic disease or risk factors for atherothrombosis, was weaker than we found at 1.33-fold. In sensitivity analyses excluding any patient with a previous ischaemic heart disease admission, we continued to observe an approximately 2-fold association. However, we did not have any measures of stable coronary disease. As such, one

explanation for the stronger association we observed is that the increased heart failure risk in diabetes is partly related explained through increased risk of atheromatous disease.

Previous studies examining case-fatality following heart failure admissions among people with type 2 diabetes have been equivocal. One multi-centre register study found no difference in in-hospital mortality among people with diabetes compared to those without (OR 1.00; 95% CI 0.88-1.14).[12] Similarly, in a study in the Scottish population comparing incident heart failure admissions from 1986-2003, the age-sex adjusted 30-day case-fatality following heart failure admission was lower in people with diabetes than in those without diabetes (for example in men aged 65 to 74 the OR was 0.82; 95% CI 0.73-0.93), although case-fatality at one-year was higher.[13] Neither study, however, included data on diabetes type. Since the majority of people with diabetes have type 2 diabetes, these reports are consistent with our own finding that people with type 2 diabetes did not have a higher case-fatality than individuals without diabetes.

Fewer studies have examined heart failure as a complication of type 1 diabetes. The largest, which was a population-based study from Sweden, and which updates and extends a previous report from the same diabetes registry,[14] reported a rate of incident heart failure hospitalisation of 6.7 per 1,000 person-years in people with type 1 diabetes compared to 4.0 per 1,000 person-years in individuals without diabetes, similar to the difference we observed.[2] However, those investigators did not examine trends over time or case-fatality. Indeed, ours is the first population-based study of which we are aware to compare case-fatality following heart failure admissions in people with and without type 1 diabetes, and we are not aware that the high case-fatality in patients with type 1 diabetes has been reported previously.

The mechanisms underlying this difference in case-fatality are unknown, and mechanistic studies are needed. Indeed, excepting coronary artery atherosclerosis, the mechanisms

underlying the relationship between diabetes and heart failure are not well understood, and whether or not diabetic cardiomyopathy represents a distinct entity or not remains controversial.[15–17] Notwithstanding the mechanisms, however, the increased case-fatality provides additional support for the view that heart failure is an under-recognised and important complication in type 1 diabetes.[18]

Time-trends in case-fatality were similar across groups. For people with and without diabetes, regardless of type, we found that case-fatality fell by around 3% per-year. We were unable to identify any previous study which compared heart failure admission case-fatality trends among people with and without diabetes. Nonetheless, similar trends have been reported in unselected patients, and in people with type 2 diabetes. In terms of the former, a study using the Swedish national hospital discharge register, which included 13.6% of people with type 2 diabetes, found a decline of approximately 4% per-year (hazard ratio 0.96 per year during the five-year period from 1987 to 2006).[19] Also, trends following heart failure admissions were examined for people with type 2 diabetes in a subset of the US National Inpatient Sample mortality (defined using administrative data - ICD-9-CM codes 250.0 to 250.9 with a fifth digit of 0 or 2). In models adjusting for age and sex, case-fatality fell by approximately 5% per year from 2000 to 2010.[20] This is consistent, therefore with our findings.

In the general adult population, a number of risk factors such as age, sex, deprivation, smoking, obesity, hypertension, cholesterol and previous cardiovascular disease are known to predict heart failure.[21] Lind et al also showed that, among people with type 1 diabetes, smoking, systolic blood pressure, high body mass index, duration of diabetes and HbA1c were associated with increased heart failure incidence.[14] We obtained similar findings for the association between these risk factors and the 3-year risk of heart failure among people with type 1 diabetes. We have

also been able to show that very similar associations (both in terms of magnitude and direction) are evident for people with type 2 as well as type 1 diabetes.

We also found that people with type 1 diabetes were less commonly prescribed drugs known to reduce the risk of heart failure, (whether directly or through reducing the risk of heart disease); this included antihypertensives, drugs acting on the renin-angiotensin system and lipid lowering drugs.[22] Importantly, these differences were still found after taking into account the fact that people with type 2 diabetes are older, and even after adjusting for each patient's predicted risk of heart failure (based on their baseline characteristics). Considerable caution is needed in interpreting this finding, as the clinical risk factors (blood pressure, smoking etc) used to adjust for baseline risk were obtained as part of routine clinical care, not in a prospective study, and were not available for some patients. Nonetheless, this observation does raise the possibility that, even where the heart failure risk is similar, people with type 1 diabetes may be less likely than people with type 2 diabetes to receive preventative drug therapy.

The strengths of our study include the very large population-based nature of the electronic record of diagnosed diabetes that captures data for >99% of the population of Scotland, information on the type of diabetes, and the availability of linkage to quality-assured hospital admission and mortality data for the whole population.[23] A limitation is that heart failure events insufficiently severe to require admission to hospital were not captured as we did not have access to primary care data.

However, we have previously shown via review by two independent clinicians (a generalist and cardiologist) that heart failure admissions in the Scottish hospitalisation database are reliably recorded.[24] Moreover, similar associations were found in a sensitivity analysis which

restricted the definition of heart failure to admission where this was coded in the first diagnostic position.

Secondly, while the data were of high quality some misclassification as a result of diagnostic uncertainty is likely to have occurred. In particular, some people with type 1 diabetes will have been classified as type 2 diabetes, and vice versa. However, there is no reason to suppose that this misclassification will have been differential by outcome, and it is therefore likely to have attenuated any observed differences between type 1 and type 2 diabetes. Indeed, in the cohort restricted to patients with diabetes in 2013, the use of a more precise definition of diabetes type did not importantly affect the estimated 3-year risk of diabetes. A further limitation is that we did not have accurate data on race or ethnicity, and so cannot comment on whether associations between diabetes and heart failure incidence differ by these variables.

Finally, we did not have access to sufficient data on left ventricular function to comment on the relative contribution of reduced and preserved ejection fraction heart failure on the differences between people with and without diabetes.

Conclusion

Despite falling incidence rates, particularly in type 1 diabetes, heart failure remains around 2-fold higher than in people without diabetes, with case-fatality also being higher in people with type 1 diabetes. Those with type 1 diabetes also received fewer preventative cardiovascular medications. These findings provide additional support for the view that heart failure is an under-recognised and important complication in diabetes, particularly among people with type 1 diabetes.

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Disclosures

PJ reports grants from Boehringer Ingelheim, during the conduct of the study; personal fees from Novartis, personal fees from Cytokinetics, personal fees from Visor Pharma, outside the submitted work. JP reports personal fees and other from Novo Nordisk, grants and personal fees from Sanofi Aventis, non-financial support from Merck (Germany), personal fees from Lilly, non-financial support from Itamar Medical, grants and personal fees from Quintiles, grants and personal fees from Janssen, personal fees from ACI Clinical, personal fees from Pfizer, outside the submitted work. NS's employer received funding from Boehringer Ingelheim for a research grant, and NS has received personal speaking fees from Boehringer Ingelheim, Novo Nordisk, Eli Lilly and Roche Diagnostics and has acted as a consultant for Boehringer Ingelheim, Janssen and Astrazeneca. JM's employer, Glasgow University, is currently or has recently been paid for his role in trials testing treatments in patients with diabetes mellitus: principal investigator DAPA-HF trial dapagliflozin AstraZeneca, principal investigator BEST trial bexagliflozin Theracos, co-principal Investigator HARMONY Outcomes trial albiglutide GSK, executive committee member DAPA-CKD trial dapagliflozin AstraZeneca, executive committee member ACE trial acarbose Oxford University/Bayer, executive committee member SONAR trial

atrasentan Abbvie, and data monitoring committee member EXSCEL trial exenatide AstraZeneca. JM's study sponsors have paid for his travel and accommodation for some meetings related to these trials. None of the other co-authors have any interest to declare.

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Table 1. Incidence of heart failure admissions stratified by age and sex

Age	Sex		No diabetes	Type 1 diabetes	Type 2 diabetes
20-29	**Men**	**Rate**	0.07 (26/354,377)	0.36 (1/2,748)	0 (0/386)
		Rate ratio	-	4.96 (0.67-36.55)	
		Rate diff.	-	0.29 (-0.42- 1.00)	-0.07 (-0.10–0.05)
	Women	**Rate**	0.08 (27/359,972)	0.46 (1/2,162)	2.18 (1/459)
		Rate ratio	-	6.17 (0.84-45.38)	29.07 (3.95-213.94)
		Rate diff.	-	0.39 (-0.52- 1.29)	2.11 (-2.17- 6.38)
30-49	**Men**	**Rate**	0.45 (309/679,479)	1.11 (7/6,304)	1.61 (23/14,260)
		Rate ratio	-	2.44 (1.15-5.17)	3.55 (2.32-5.42)
		Rate diff.	-	0.66 (-0.17- 1.48)	1.16 (0.50-1.82)
	Women	**Rate**	0.2 (144/721,321)	1.54 (7/4,555)	1.5 (15/9,984)
		Rate ratio	-	7.70 (3.61-16.44)	7.53 (4.42-12.81)
		Rate diff.	-	1.34 (0.20-2.48)	1.30 (0.54-2.06)
50-69	**Men**	**Rate**	2.31 (1360/587,720)	8.26 (38/4,599)	6.88 (452/65,712)
		Rate ratio	-	3.57 (2.59-4.93)	2.97 (2.67-3.31)
		Rate diff.	-	5.95 (3.32-8.58)	4.56 (3.92-5.21)
	Women	**Rate**	1.09 (702/645,356)	6.23 (21/3,371)	5.25 (231/43,998)
		Rate ratio	-	5.73 (3.71-8.84)	4.83 (4.16-5.60)
		Rate diff.	-	5.14 (2.48-7.81)	4.16 (3.48-4.84)
70-89	**Men**	**Rate**	12.68 (2832/223,396)	31.4 (27/860)	22.21 (994/44,756)
		Rate ratio	-	2.48 (1.70-3.62)	1.75 (1.63-1.88)
		Rate diff.	-	18.72 (6.87-30.57)	9.53 (8.07-10.99)
	Women	**Rate**	10.26 (3361/327,652)	30.65 (31/1,011)	19.75 (914/46,277)
		Rate ratio	-	2.99 (2.10-4.26)	1.93 (1.79-2.07)
		Rate diff.	-	20.39 (9.60-31.19)	9.49 (8.17-10.82)

Rates and rate differences are per 1,000 person year, rate ratios and rate differences are reported with 95% confidence intervals.

Table 2. 30-day case-fatality of incident heart failure hospitalisation, by age and sex

Age	Sex	No diabetes	Type 1 diabetes	Type 2 diabetes
20-39	Men	4.0% (8/199)	10.0% (1/10)	0.0% (0/4)
	Women	4.6% (6/130)	0.0% (0/7)	0.0% (0/5)
30-49	Men	4.4% (131/2953)	9.3% (10/107)	3.1% (8/258)
	Women	7.8% (97/1248)	8.8% (6/68)	6.2% (8/129)
50-69	Men	6.9% (974/14175)	13.6% (43/316)	7.3% (305/4151)
	Women	10.0% (721/7242)	10.6% (25/236)	9.4% (196/2082)
70-89	Men	16.5% (4795/29013)	23.0% (63/274)	14.6% (1216/8318)
	Women	17.7% (6462/36469)	18.3% (54/295)	15.9% (1277/8012)
All	Men	12.7% (5908/46340)	16.5% (117/707)	12.0% (1529/12731)
	Women	16.2% (7286/45089)	14.0% (85/606)	14.5% (1481/10228)

Case-fatality shown as percentages (deaths/admissions).

Table 3. Risk factors for heart failure in people with diabetes. Summary statistics, association with incident heart failure hospitalisation within three years and comparison of association in type 1 versus type 2 diabetes

Risk factor	Summary statistics		Heart failure risk factors stratified		Heart failure risk factors comparison	
	Type 1	Type 2	Type 1	Type 2	Type 1/Type 2	P-value
N	26189	288208				
Age (years)	45 (15)	65 (13)	1.85 (1.57-2.19)	1.99 (1.91-2.07)	0.93 (0.78-1.11)	0.42
Male	14907 (56.9%)	162029 (56.2%)	1.05 (0.79-1.40)	1.16 (1.09-1.22)	0.91 (0.68-1.22)	0.52
Deprivation (Deciles)	5 (3 to 8)	5 (3 to 7)	1.14 (0.99-1.32)	1.10 (1.06-1.12)	1.04 (0.90-1.20)	0.57
Body mass index (kg/m2)	26 (24 to 30)	31 (28 to 35)	1.22 (1.04-1.45)	1.26 (1.23-1.30)	0.97 (0.82-1.15)	0.74
Never smoker	13047 (54.7%)	113952 (43.6%)	1	1	1	-
Ex-smoker	4510 (18.9%)	92826 (35.5%)	1.91 (1.38-2.63)	1.22 (1.15-1.30)	1.56 (1.12-2.16)	0.008
Current smoker	6297 (26.4%)	54874 (21%)	2.04 (1.42-2.93)	1.59 (1.48-1.71)	1.28 (0.88-1.86)	0.20
Systolic blood pressure (mmHg)	130 (13)	136 (13)	1.06 (0.93-1.20)	1.08 (1.05-1.11)	0.98 (0.86-1.11)	0.73
Diastolic blood pressure (mmHg)	75 (8)	77 (8)	-	-	-	-
Total cholesterol (mg/dL)	4.7 (1)	4.4 (1)	1.30 (1.15-1.48)	0.99 (0.96-1.02)	1.32 (1.16-1.51)	<0.001
LDL cholesterol (mg/dL)	2.5 (0.8)	2.3 (0.9)	-	-	-	-
HDL cholesterol (mg/dL)	1.5 (0.4)	1.2 (0.3)	0.90 (0.79-1.02)	1.00 (0.97-1.03)	0.90 (0.79-1.02)	0.10
HbA1c (mmol/mol)	71 (62 to 83)	56 (48 to 67)	1.32 (1.16-1.51)	1.17 (1.13-1.20)	1.13 (0.99-1.29)	0.06
Estimated glomerular filtration rate (ml/min)	98 (83 to 110)	81 (65 to 93)	0.65 (0.56-0.75)	0.72 (0.70-0.74)	0.90 (0.77-1.05)	0.17
Previous stroke	275 (29.3%)	7278 (26.7%)	1.93 (1.09-3.40)	1.36 (1.21-1.52)	1.42 (0.80-2.53)	0.24
Previous myocardial infarction	585 (62.4%)	18224 (66.7%)	1.60 (1.03-2.49)	1.68 (1.56-1.80)	0.96 (0.61-1.50)	0.84
Duration of diabetes (years)	19 (10 to 30)	5 (1 to 11)	1.29 (1.18-1.40)	1.17 (1.14-1.20)	1.10 (1.01-1.20)	0.04
Retinopathy	7900 (30.2%)	36410 (12.6%)	0.66 (0.48-0.92)	1.15 (1.07-1.23)	0.58 (0.41-0.80)	0.001

Summary statistics are the number (percentage), mean (standard deviation), and median (interquartile range) for risk factors which are categorical, symmetrical and skewed continuous variables respectively. The odds ratios (and 95% confidence intervals) are for the odds of heart failure within 3-years for people with type 1 and type 2 diabetes, along with an interaction odds ratio for the difference in odds ratio between people with type 1 and type 2 diabetes. The P-value for the interaction is also shown. Deprivation is coded from least to most deprived. All continuous variables were standardised so that the odds ratio can be interpreted as the increase in odds per standard deviation increment. All variables in the table were included in the model with the exception of LDL cholesterol because this was not measured in large proportion of patients, and diastolic blood pressure because this is likely to be collinear with systolic blood pressure. The extent of missing data and approach to missingness are documented in the supplementary appendix.

Table 4 Cardiovascular drugs in people with diabetes

	Summary statistics		Odds ratio for drug prescription in type 2 versus type 1		
Drug	Type 1	Type 2	Unadjusted	Model 1	Model 2
Thiazides	1349 (5.2%)	47228 (16.4%)	3.61 (3.41-3.82)	2.17 (2.04-2.29)	2.11 (1.99-2.23)
Loop	1174 (4.5%)	31623 (11%)	2.63 (2.47-2.79)	0.87 (0.82-0.93)	0.88 (0.82-0.94)
Potassium sparing	197 (0.8%)	7055 (2.4%)	3.31 (2.87-3.82)	1.78 (1.53-2.05)	1.68 (1.45-1.94)
Beta blockers	1996 (7.6%)	75105 (26.1%)	4.27 (4.08-4.47)	2.15 (2.05-2.25)	1.97 (1.88-2.07)
Renin-Angiotensin System Drugs	7563 (28.9%)	145304 (50.4%)	2.50 (2.44-2.57)	1.33 (1.29-1.37)	1.14 (1.1-1.17)
Nitrates and other anti-anginal	653 (2.5%)	24183 (8.4%)	3.58 (3.31-3.88)	1.55 (1.43-1.68)	1.50 (1.38-1.63)
Calcium-Channel Blockers	2637 (10.1%)	72817 (25.3%)	3.02 (2.9-3.15)	1.59 (1.52-1.66)	1.48 (1.41-1.54)
Anticoagulants	249 (1%)	14386 (5%)	5.47 (4.83-6.21)	1.82 (1.6-2.07)	1.74 (1.53-1.98)
Antiplatelets	4079 (15.6%)	94631 (32.8%)	2.65 (2.56-2.74)	1.03 (0.99-1.07)	0.90 (0.87-0.94)
Lipid lowering drugs	9222 (35.2%)	178100 (61.8%)	2.98 (2.9-3.06)	1.39 (1.35-1.43)	1.21 (1.18-1.25)

N (%) of people currently prescribed at least one drug the relevant class at the start of the closed cohort, October 1st 2013. Odds ratios (95% CIs) that drug is prescribed in people with type 2 versus type 1 diabetes. Each drug-class was modelled separately, unadjusted, adjusted for age and sex (model 1) and adjusted for the predicted risk of heart failure (model 2). The predicted risk in model 2 was obtained from the full set of model coefficients for the full models shown in Table 3, and hence is based on each patient's baseline characteristics (age, sex, deprivation, duration of diabetes, body mass index, smoking status, previous stroke, previous myocardial infarction, systolic blood pressure total and HDL cholesterol, HbA1c, estimated glomerular filtration rate and retinopathy). See supplementary appendix for the approach used to classify drugs.

Figure Legends

Figure 1. Age, sex and deprivation adjusted incidence of heart failure hospitalisation by diabetes type, age and sex

The lines represent the predicted rates obtained from quasi-Poisson regression models of incident heart failure events. The ribbons are 95% confidence intervals. Covariates included in the model were age, sex, deprivation and diabetes type, with interaction terms included where these improved model fit. Predictions were made at the median deprivation score. Points represent event rates stratified by age (in years), sex and diabetes type. Models are given in full in the supplementary appendix.

Figure 2. Age, sex and deprivation adjusted trends in incident heart failure hospitalisation by diabetes type, sex and calendar-year

The lines represent the predicted rates obtained from generalized additive models of incident heart failure events. The ribbons are 95% confidence intervals. Covariates included in the model were age, sex, deprivation, diabetes type and calendar-year, with interaction terms included where these improved model fit. The model was fit with a log-link and Poisson likelihood, with correction of the standard errors for overdispersion. Penalized thin plate regression splines were used to model non-linear associations for calendar-year by diagnosis type. Predictions were made for men and women aged 50 (as this was the closest decade to the mean age in the general population). Models are given in full in the supplementary appendix. See https://ihwph-hehta.shinyapps.io/dm_hf_fig2/ for an interactive version of this plot.

Figure 3. Age, sex and deprivation adjusted 30-day case-fatality of incident heart failure hospitalisation by age, sex and diabetes type

The lines represent the predicted case-fatality proportions obtained from logistic regression models of death. Covariates included in the model were age, sex, deprivation and diabetes type, with interaction terms included where these improved model fit. Predictions were made at the median deprivation score. Points represent case-fatality proportions stratified by age, sex and diabetes type, with the point size being proportional to the number in the denominator. Models are given in full in the supplementary appendix.

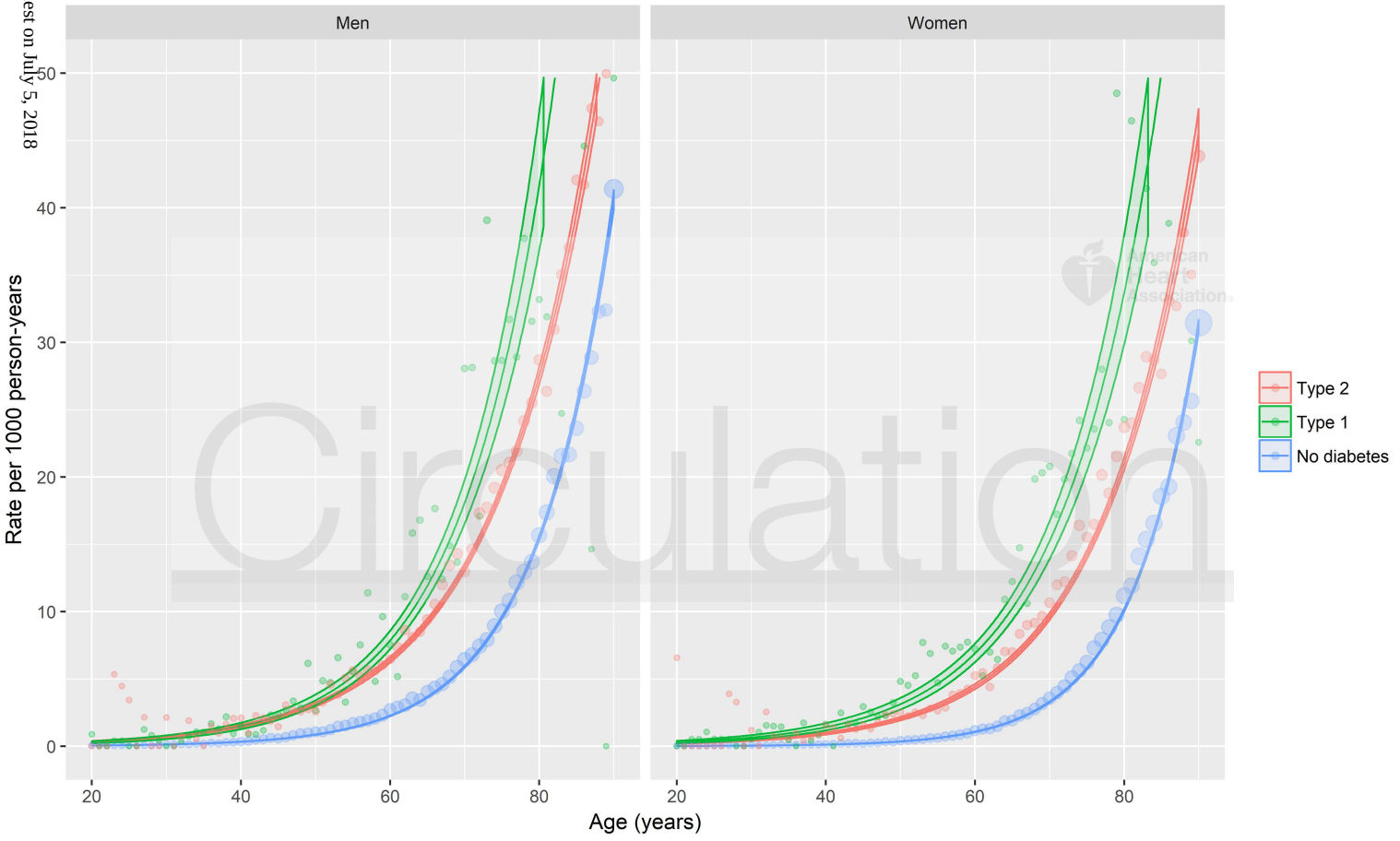
Figure 4. Age, sex and deprivation adjusted trends in 30-day case-fatality of incident heart failure hospitalisation

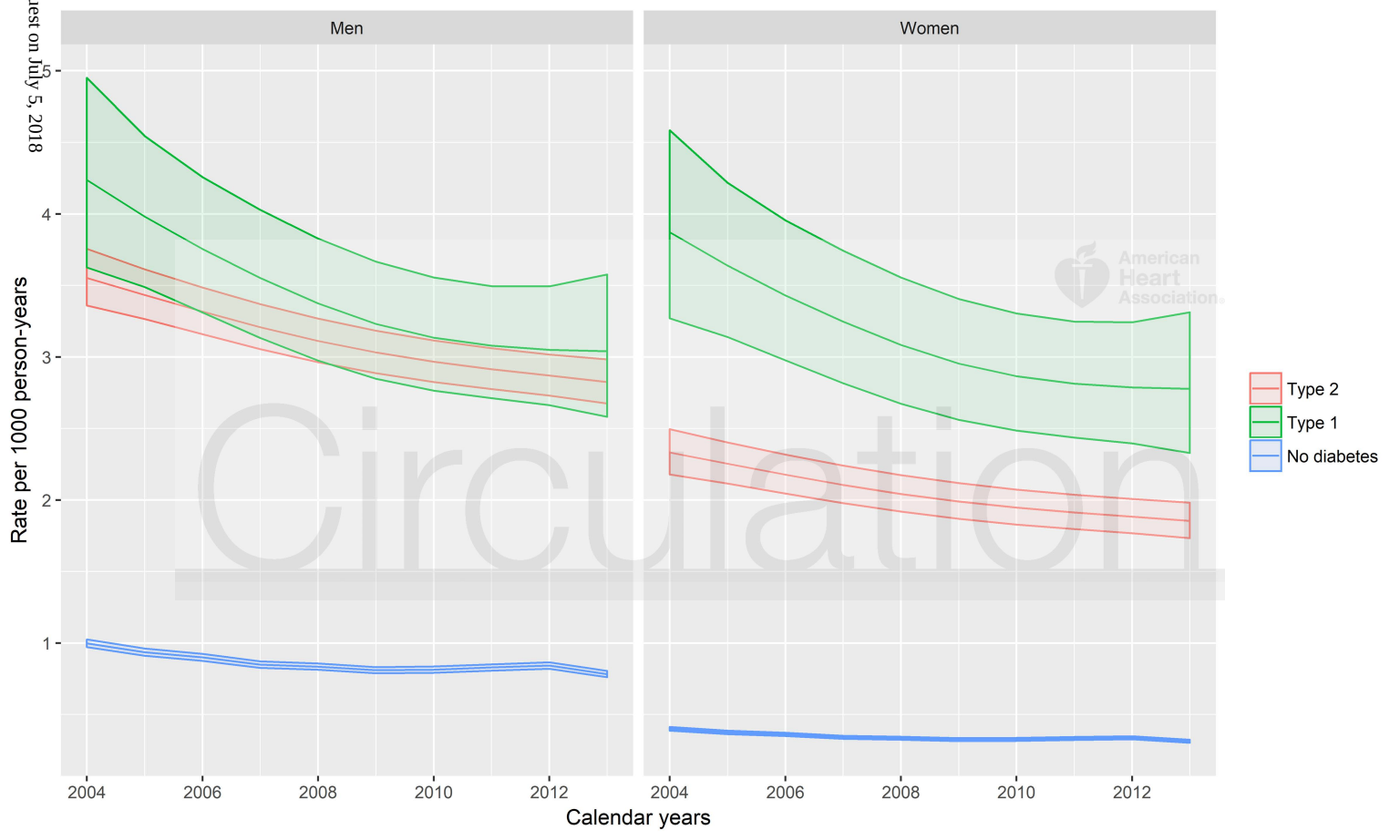
The lines represent the predicted rates obtained from generalized additive models of heart failure 30-day case-fatality on age, sex, deprivation, diabetes type and calendar-year, with interaction terms included where these improved model fit, using a logit-link and binomial likelihood. Predictions were made for men and women aged 50 (as this was the closest decade to the mean age in the general population). Models are given in full in the supplementary appendix.

Figure 5. Age, sex and deprivation adjusted incidence of heart failure hospitalisation by diabetes type, age and sex in people without previous ischaemic heart disease

The lines represent the predicted rates obtained from quasi-Poisson regression models of incident heart failure events. The ribbons are 95% confidence intervals. Covariates included in the model were age, sex, deprivation and diabetes type, with interaction terms included where these improved model fit. Predictions were made at the median deprivation score. Points represent

event rates stratified by age (in years), sex and diabetes type. Models are given in full in the supplementary appendix.




Men
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Rate per 1000 person-years
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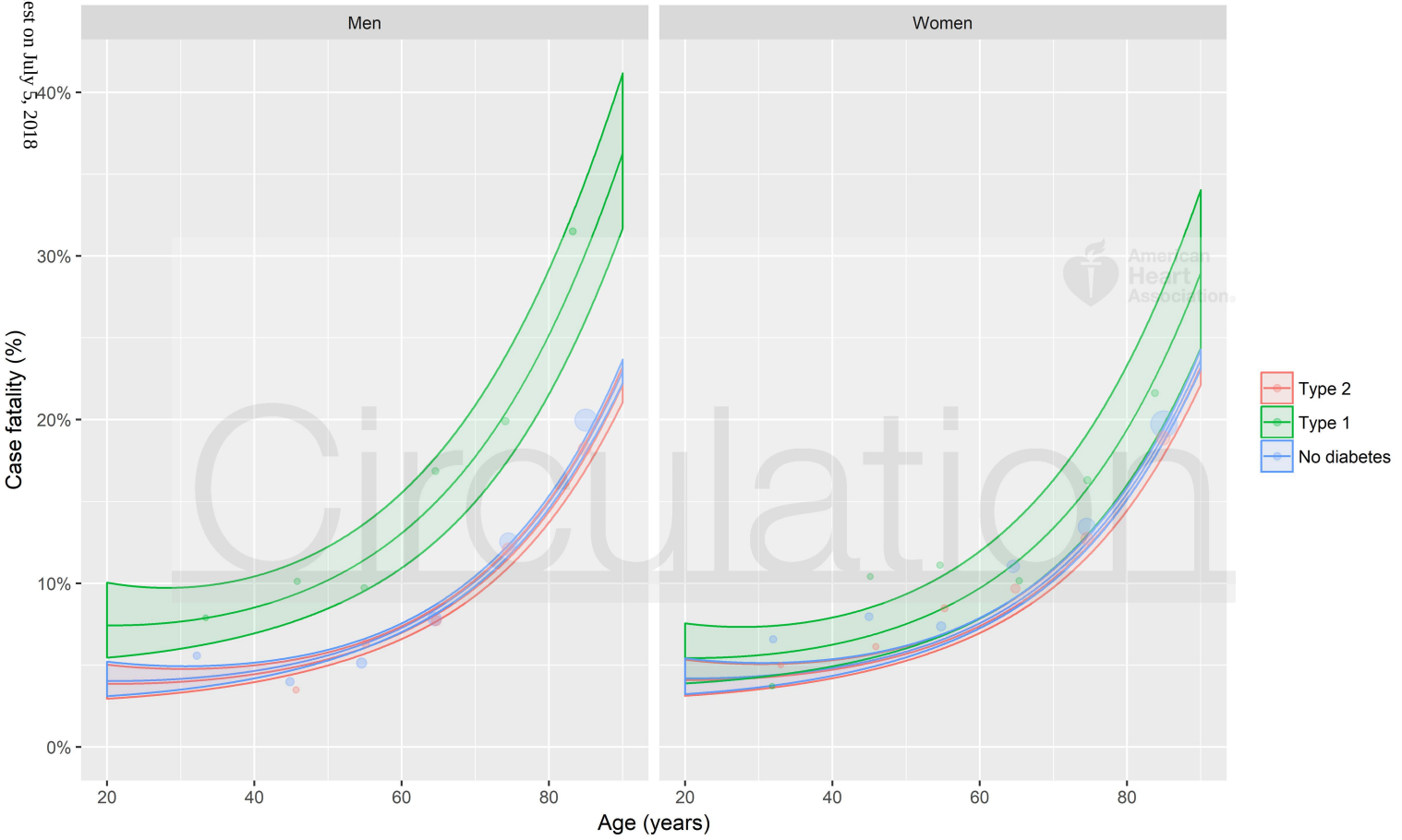
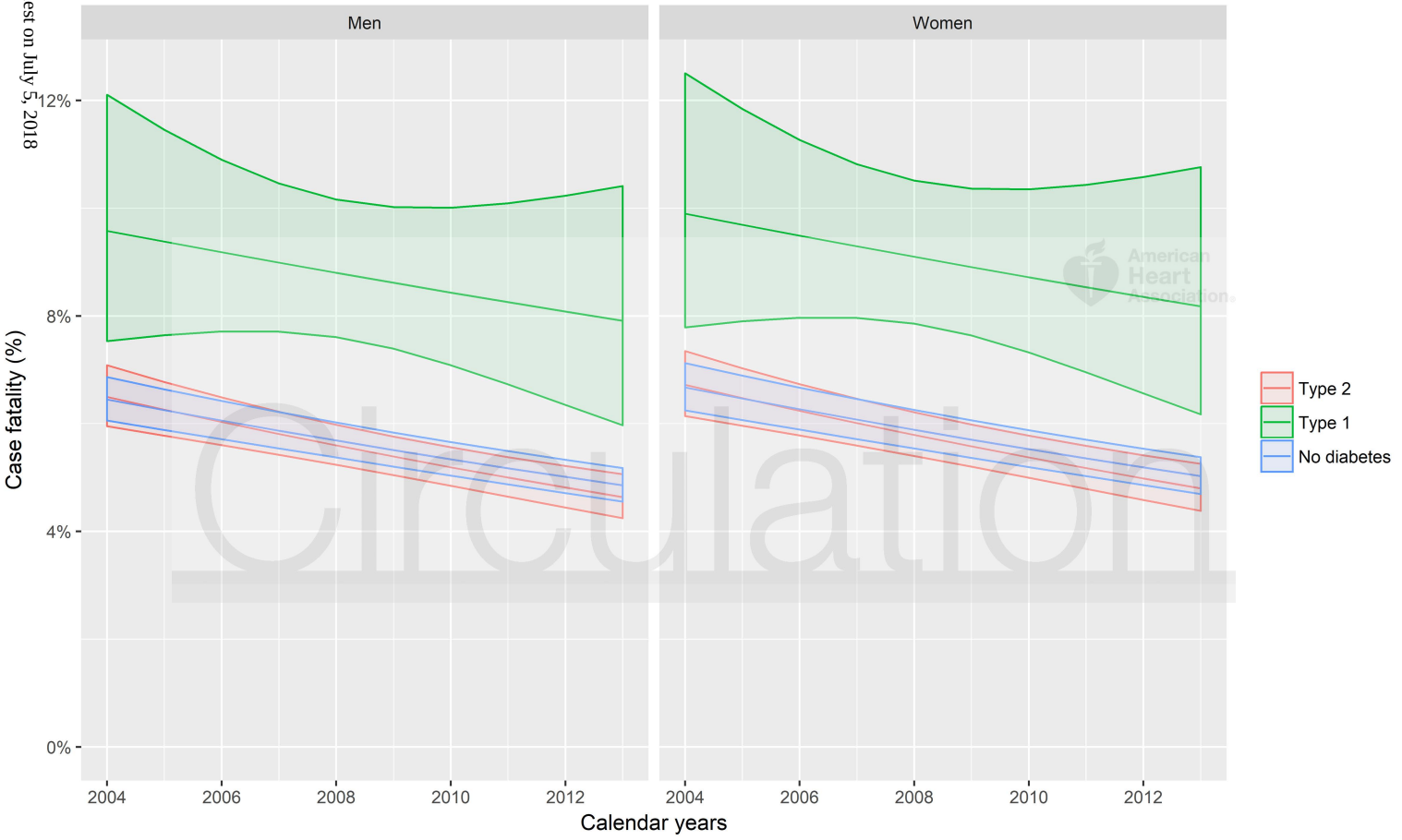
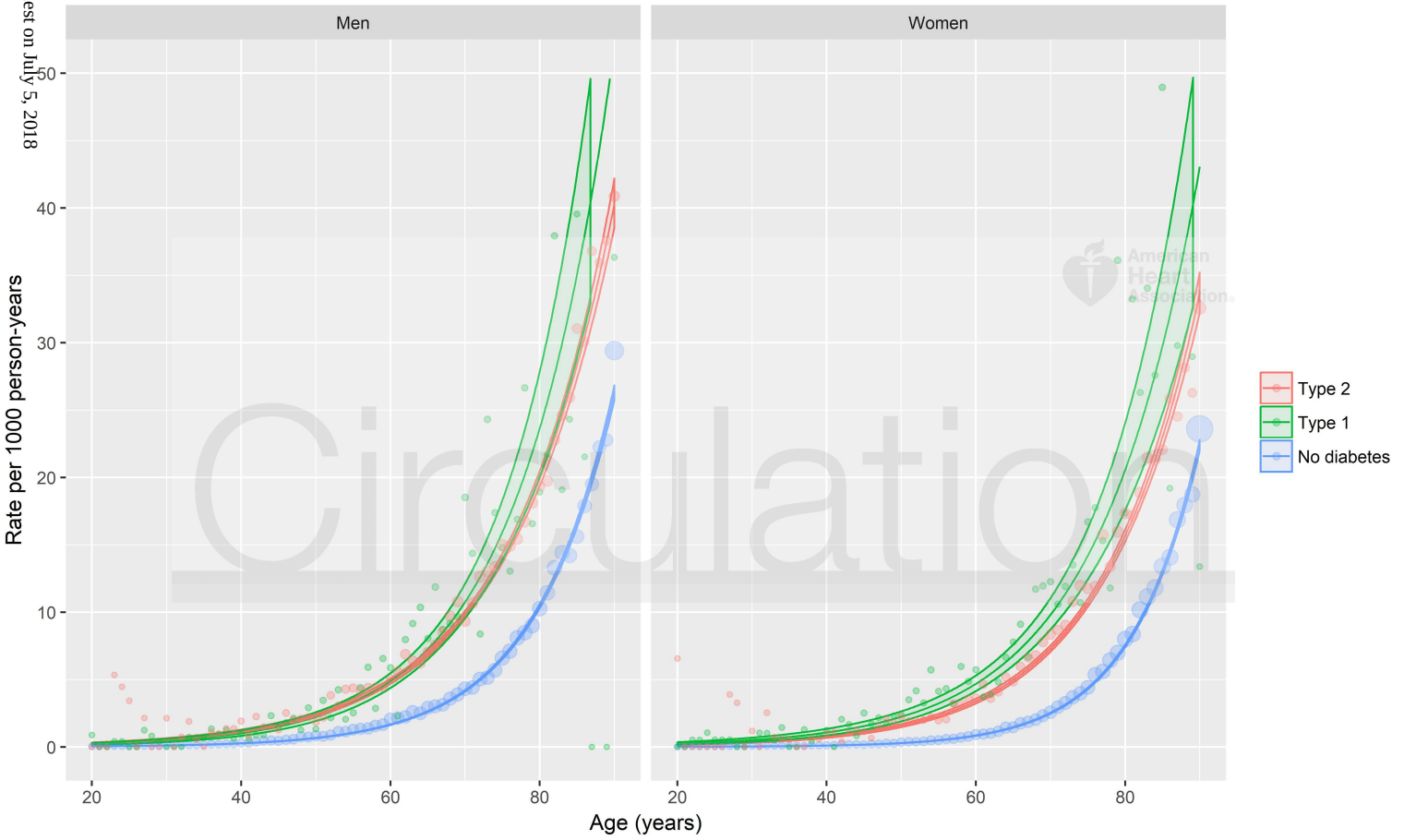
Type 2
Type 1
No diabetes
Circulation
American Heart Association







Incidence of Hospitalisation for Heart Failure and Case-Fatality Among 3.25 Million People with and without Diabetes

David A. McAllister, Stephanie Read, Jan Kerssens, Shona Livingstone, Stuart McGurnaghan, Pardeep Jhund, John Petrie, Naveed Sattar, Colin Fischbacher, Soren L Kristensen, John McMurray, Helen M. Colhoun and Sarah Wild

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SUPPLEMENTAL MATERIAL

Incidence of hospitalisation for heart failure and case-fatality among 3.25 million people with and without diabetes

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Contents

Aggregated data

Table S1 Heart failure admissions by age, sex, deprivation and diagnosis

Age	Sex	Deprivation	Diagnosis	Admissions	Persontime
20 to 49	men	1-5	No diabetes	1087	5069751
20 to 49	men	1-5	Type1	40	41394
20 to 49	men	1-5	Type 2	86	49255
20 to 49	men	6-10	No diabetes	2065	5263772
20 to 49	men	6-10	Type1	77	44487
20 to 49	men	6-10	Type 2	176	76730
20 to 49	women	1-5	No diabetes	433	5249525
20 to 49	women	1-5	Type1	29	30875
20 to 49	women	1-5	Type 2	31	31915
20 to 49	women	6-10	No diabetes	945	5601676
20 to 49	women	6-10	Type1	46	32760
20 to 49	women	6-10	Type 2	103	58611
50 to 59	men	1-5	No diabetes	2055	1693189
50 to 59	men	1-5	Type1	46	12610
50 to 59	men	1-5	Type 2	385	99307

Age	Sex	Deprivation	Diagnosis	Admissions	Persontime
50 to 59	men	6-10	No diabetes	2955	1458296
50 to 59	men	6-10	Type1	98	11905
50 to 59	men	6-10	Type 2	708	123769
50 to 59	women	1-5	No diabetes	704	1794524
50 to 59	women	1-5	Type1	39	8931
50 to 59	women	1-5	Type 2	145	56955
50 to 59	women	6-10	No diabetes	1416	1569962
50 to 59	women	6-10	Type1	69	8380
50 to 59	women	6-10	Type 2	303	87522
60 to 69	men	1-5	No diabetes	3812	1263936
60 to 69	men	1-5	Type1	75	7191
60 to 69	men	1-5	Type 2	1175	145099
60 to 69	men	6-10	No diabetes	5353	1124748
60 to 69	men	6-10	Type1	97	6804
60 to 69	men	6-10	Type 2	1883	163745
60 to 69	women	1-5	No diabetes	1865	1411898
60 to 69	women	1-5	Type1	49	6010
60 to 69	women	1-5	Type 2	500	92678
60 to 69	women	6-10	No diabetes	3257	1287385
60 to 69	women	6-10	Type1	79	5690
60 to 69	women	6-10	Type 2	1134	132674
70 to 79	men	1-5	No diabetes	5934	741182
70 to 79	men	1-5	Type1	87	3469
70 to 79	men	1-5	Type 2	2121	121589
70 to 79	men	6-10	No diabetes	7511	704085
70 to 79	men	6-10	Type1	114	3372
70 to 79	men	6-10	Type 2	2743	135025
70 to 79	women	1-5	No diabetes	4479	943917
70 to 79	women	1-5	Type1	82	3766
70 to 79	women	1-5	Type 2	1383	103576
70 to 79	women	6-10	No diabetes	7232	987117
70 to 79	women	6-10	Type1	102	3962
70 to 79	women	6-10	Type 2	2445	142301
80 to 89	men	1-5	No diabetes	7690	339174
80 to 89	men	1-5	Type1	35	899
80 to 89	men	1-5	Type 2	1737	49383
80 to 89	men	6-10	No diabetes	7878	314140
80 to 89	men	6-10	Type1	38	833
80 to 89	men	6-10	Type 2	1717	46507
80 to 89	women	1-5	No diabetes	11513	640946
80 to 89	women	1-5	Type1	48	1251
80 to 89	women	1-5	Type 2	1843	64392
80 to 89	women	6-10	No diabetes	13245	653518
80 to 89	women	6-10	Type1	63	1334
80 to 89	women	6-10	Type 2	2341	74249

Numbers less than or equal to 5 were suppressed to maintain confidentiality.

Table S2 Heart failure deaths within 30 days of admission by age, sex, deprivation and diagnosis

Age	Sex	Deprivation	Diagnosis	Admissions	Deaths
20 to 29	men	1-5	pop	75	<=5
20 to 29	men	1-5	t1dm	<=5	<=5
20 to 29	men	1-5	t2dm	<=5	<=5
20 to 29	men	6-10	pop	124	<=5
20 to 29	men	6-10	t1dm	6	<=5
20 to 29	men	6-10	t2dm	<=5	<=5
20 to 29	women	1-5	pop	51	<=5
20 to 29	women	1-5	t1dm	<=5	<=5
20 to 29	women	6-10	pop	79	<=5
20 to 29	women	6-10	t1dm	<=5	<=5
20 to 29	women	6-10	t2dm	<=5	<=5
30 to 49	men	1-5	pop	1012	31
30 to 49	men	1-5	t1dm	36	6
30 to 49	men	1-5	t2dm	85	<=5
30 to 49	men	6-10	pop	1941	100
30 to 49	men	6-10	t1dm	71	<=5
30 to 49	men	6-10	t2dm	173	<=5
30 to 49	women	1-5	pop	382	26
30 to 49	women	1-5	t1dm	27	<=5
30 to 49	women	1-5	t2dm	31	<=5
30 to 49	women	6-10	pop	866	71
30 to 49	women	6-10	t1dm	41	<=5
30 to 49	women	6-10	t2dm	98	6
50 to 59	men	1-5	pop	2055	76
50 to 59	men	1-5	t1dm	46	<=5
50 to 59	men	1-5	t2dm	385	23
50 to 59	men	6-10	pop	2955	181
50 to 59	men	6-10	t1dm	98	10
50 to 59	men	6-10	t2dm	708	46
50 to 59	women	1-5	pop	704	30
50 to 59	women	1-5	t1dm	39	<=5
50 to 59	women	1-5	t2dm	145	10
50 to 59	women	6-10	pop	1416	126
50 to 59	women	6-10	t1dm	69	7
50 to 59	women	6-10	t2dm	303	28
60 to 69	men	1-5	pop	3812	264
60 to 69	men	1-5	t1dm	75	14
60 to 69	men	1-5	t2dm	1175	76
60 to 69	men	6-10	pop	5353	453
60 to 69	men	6-10	t1dm	97	15
60 to 69	men	6-10	t2dm	1883	160
60 to 69	women	1-5	pop	1865	175
60 to 69	women	1-5	t1dm	49	<=5
60 to 69	women	1-5	t2dm	500	39
60 to 69	women	6-10	pop	3257	390
60 to 69	women	6-10	t1dm	79	10
60 to 69	women	6-10	t2dm	1134	119
70 to 79	men	1-5	pop	5934	684
70 to 79	men	1-5	t1dm	87	17
70 to 79	men	1-5	t2dm	2121	261
70 to 79	men	6-10	pop	7511	1001
70 to 79	men	6-10	t1dm	114	23

Age	Sex	Deprivation	Diagnosis	Admissions	Deaths
70 to 79	men	6-10	t2dm	2743	326
70 to 79	women	1-5	pop	4479	578
70 to 79	women	1-5	t1dm	82	17
70 to 79	women	1-5	t2dm	1383	166
70 to 79	women	6-10	pop	7232	997
70 to 79	women	6-10	t1dm	102	13
70 to 79	women	6-10	t2dm	2445	321
80 to 89	men	1-5	pop	7690	1531
80 to 89	men	1-5	t1dm	35	10
80 to 89	men	1-5	t2dm	1737	307
80 to 89	men	6-10	pop	7878	1579
80 to 89	men	6-10	t1dm	38	13
80 to 89	men	6-10	t2dm	1717	322
80 to 89	women	1-5	pop	11513	2260
80 to 89	women	1-5	t1dm	48	10
80 to 89	women	1-5	t2dm	1843	350
80 to 89	women	6-10	pop	13245	2627
80 to 89	women	6-10	t1dm	63	14
80 to 89	women	6-10	t2dm	2341	440

Classification of drugs

All drugs for people with diabetes are incldued in the Scottish diabetes register, having been extracted from primary care records. These are assigned to a British National Formulary (BNF) chapter, section and paragraph heading. We collapsed the BNF headings to each of the groups shown in Table S3. See https://openprescribing.net/bnf/ for a complete list of headings. Patients were counted as having been prescribed the drug if they were currently prescribed a drug within that class on the cohort start date, the 1st of October 2013.

Table S3 Prescribed drugs, groups each BNF heading assigned to

BNF heading	BNF heading label	Group
2.2.1	Thiazides And Related Diuretics	Thiazides
2.2.2	Loop Diuretics	Loop
2.2.3	Pot-Sparing Diuretics&Aldosterone Antag	Potassium sparing
2.2.4	Potassium Sparing Diuretics & Compounds	Potassium sparing
2.4	Beta-Adrenoceptor Blocking Drugs	Beta blockers
2.5.5	Renin-Angiotensin System Drugs	Renin-Angiotensin System Drugs
2.6.1	Nitrates	Nitrates and other anti-anginal
2.6.2	Calcium-Channel Blockers	Calcium-Channel Blockers
2.6.3	Other Antianginal Drugs	Nitrates and other anti-anginal
2.8.2	Oral Anticoagulants	Anticoagulants
2.9	Antiplatelet Drugs	Antiplatelets
2.12	Lipid-Regulating Drugs	Lipid lowering drugs

Incidence rate calculation using a look-back period

Figure S1 shows a worked example for the calculation of events and person-time for a notional population stratum. For example, men born in 1968 who did not have diabetes. In this example, 3 people had one or more admission with heart failure during the follow-up period, and/or during the 10 year look-back period. The calculation of year-specific incident counts is straightforward, and is shown alongside the figure. Any event after the start of the cohort period, where there was no previous event within 10 years is considered incident and this is summed across rows.

The person-years calculation is more complex and is shown in Tables S4 and S5.

Figure S1 Admissions and incident events in 3 example patients

	One		Two		Three		Total
	A	I	A	I	A	I	I
1994							
1995	1	0					
1996							
1997							
1998							
1999							
2000							
2001							
2002							
2003					1	0	
2004							0
2005							0
2006							0
2007							0
2008							0
2009							0
2010							0
2011	1	1	1	1			2
2012							0
2013							0

A - admission, I incident event.

Table S4 components of person time calculation

Year	POP	DM	p1	p2	p3
2004	190	10	0	1	0
2005	190	10	0	1	0
2006	190	10	1	1	0
2007	190	10	1	1	0
2008	190	10	1	1	0
2009	190	12	1	1	0
2010	190	12	1	1	0
2011	185	12	0	0	0
2012	185	12	0	0	0
2013	185	13	0	0	1

POP refers to the mid-year estimate for the population (based on National Records Scotland census data and mid-year estimation modelling). DM refers to the population with diabetes (from the diabetes register) and p1, p2 and p3 refers to the person-time for the 3 patients.

Since patient 1 had an admission in 1995, they were not eligible to have another incident event within ten years, and so the person-time for each of these periods is removed. Patient 2 had an incident event in 2011 and so only contributed 7 person-years. Patient 3 had an event in 2003 which was not incident, and as a consequence contributed only one person year.

The person-time for each year, within each stratum, is calculated as follows:-

$$PT = POP - DM - N + p_1 + p_2 + p_3 + ...p_n$$

Where POP, DM and p_n are as per Table S4 and N indicates the number of patients with events observed.

In R, for this example, this would be calculated as follows, along with the calendar-year/stratum-specific rate.

```
pt_ill2 <- pt_ill %>%
  mutate(`Person time` = POP - DM - 3 + p1 + p2 + p3,
         `Rate per 1000 person-years` = 1000* Incident/`Person time`)
```

Table S5 person time and rate calculation

Year	POP	DM	p1	p2	p3	Incident	Person time	Rate per 1000 person-years
2004	190	10	0	1	0	0	178	0.0
2005	190	10	0	1	0	0	178	0.0
2006	190	10	1	1	0	0	179	0.0
2007	190	10	1	1	0	0	179	0.0
2008	190	10	1	1	0	0	179	0.0
2009	190	12	1	1	0	0	177	0.0
2010	190	12	1	1	0	0	177	0.0
2011	185	12	0	0	0	2	170	11.8
2012	185	12	0	0	0	0	170	0.0
2013	185	13	0	0	1	0	170	0.0

Missing data and imputation for risk factor data

For the cohort with diabetes identified in 2013, there was missing data for a number of variables (Table S6).

Table S6 Proportion of missing data for each variable for the 2013 cohort of people with type 1 and type 2 diabetes, used to estimate associations with clinical risk factors

	Type 2	Type 1
Age	0%	0%
BMI	20.1%	16.4%
Deprivation (Deciles)	0%	0%
Diastolic BP	7.5%	9.1%
EGFR	39.8%	42.5%
HbA1	17.6%	11.2%
HDL	18.8%	19.2%
LDL	71.1%	57.9%
Retinopathy	0%	0%
Sex	0%	0%
Smoking status	9.2%	8.9%
Systolic BP	7.5%	9.1%
Total cholesterol	11.1%	13%

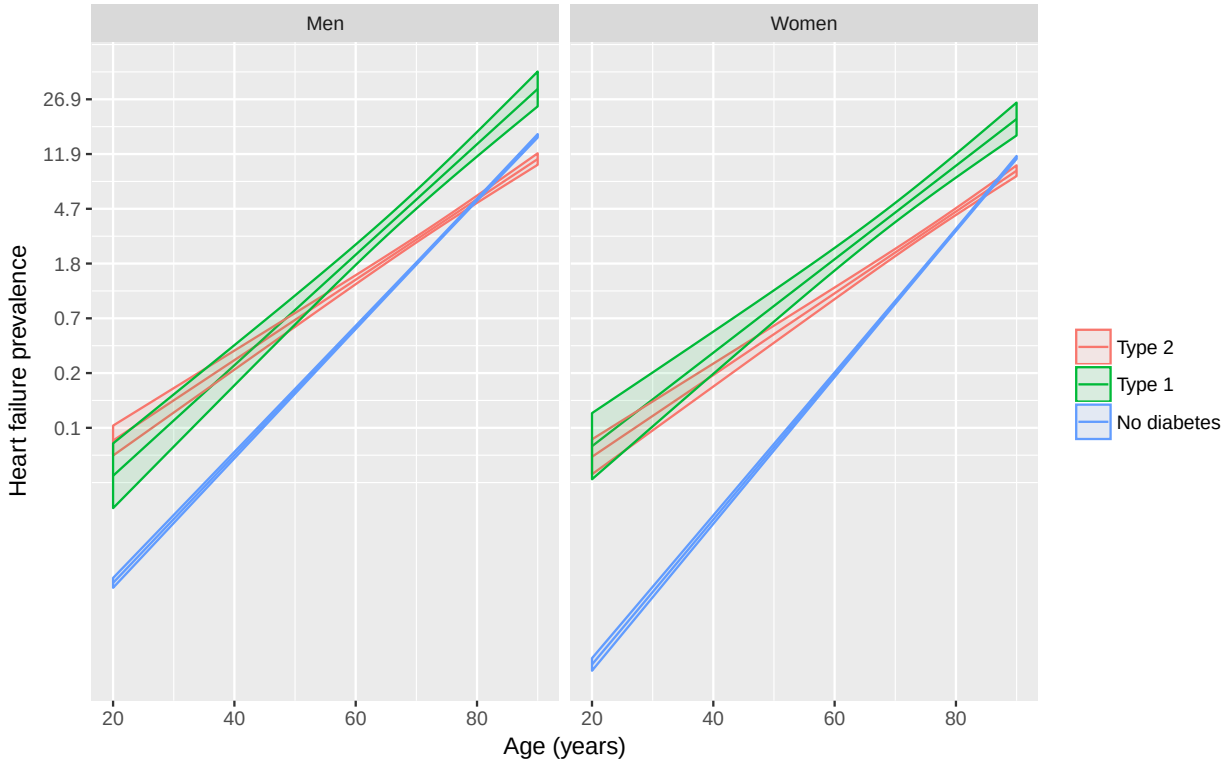
Summary statistics for each variable are reported (in Table 3 in the main manuscript) based on the available data for each variable. For the logistic regression models, we carried out multiple imputation, using the MICE package in R.[1]

We obtained 5 imputed datasets, using all the variables included in the planned model as well as LDL cholesterol and diastolic blood pressure. Imputation was performed using the following methods for each variable-type:- predictive mean matching for continuous variables, logistic regression for binary variables, polytomous regression for unordered categorical variables and proportional odds model for ordered categorical variables.

We then fit a logistic regression model to each imputed dataset and pooled the results using the method described by Barnard and Rubin.[2] Results of the modelling are shown in Table 3 of the main manscript.

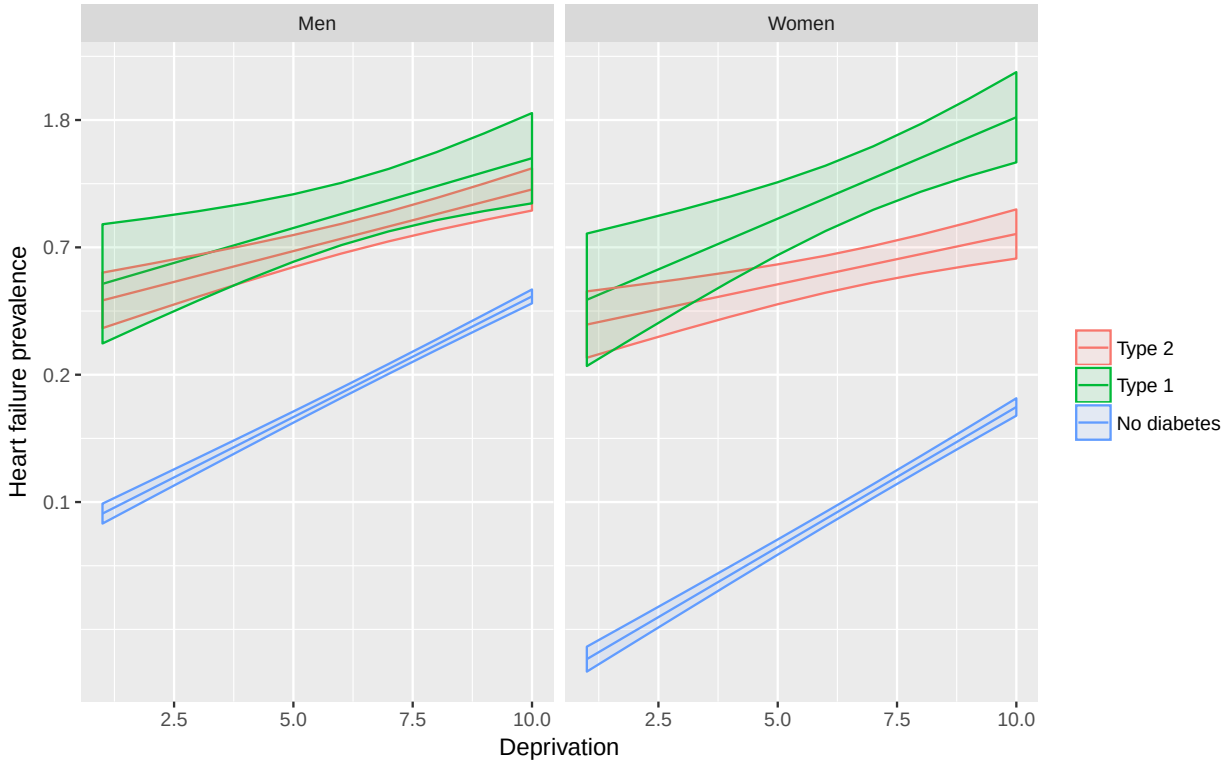
Main analysis - additional tables and figures

Figure S2 Prevalence of heart failure by diabetes type, age and sex



The lines represent the predicted prevalences obtained from logistic regression models of prevalent heart failure events on age, sex, deprivation and diabetes type, with interaction terms included where these improved model fit. Predictions were made at the median deprivation score.

Figure S3 Prevalence of heart failure by diabetes type, deprivation and sex



The lines represent the predicted prevalences obtained from logistic regression models of prevalent heart failure events on age, sex, deprivation and diabetes type, with interaction terms included where these improved model fit. Predictions were made at age 50.

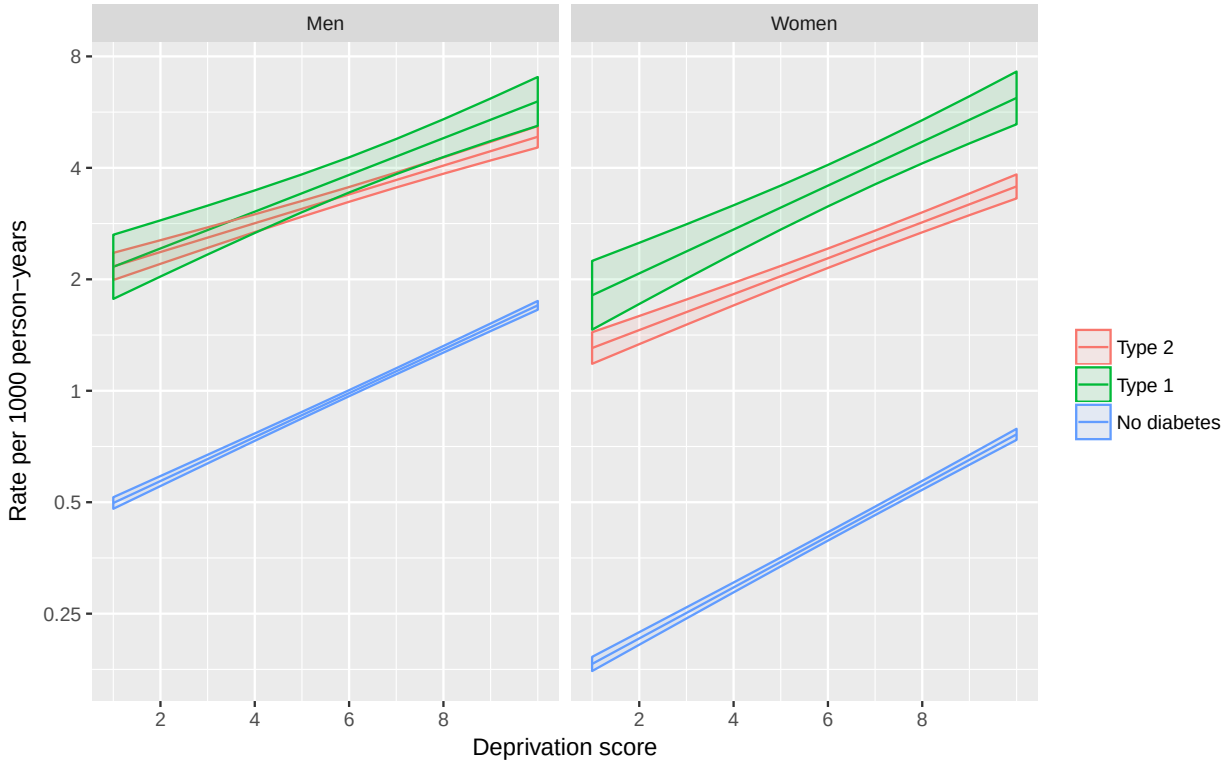
Table S7 Cross-sectional prevalence model, coefficients and standard errors

	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-7.28	0.045	-161.023	<0.001
age_ten	1.371	0.016	87.729	<0.001
sex	-1.173	0.048	-24.383	<0.001
dep_two	0.948	0.03	31.527	<0.001
typet1dm	1.884	0.275	6.846	<0.001
typet2dm	1.767	0.134	13.194	<0.001
age_ten:sex	0.156	0.012	13.405	<0.001
age_ten:dep_two	-0.205	0.01	-19.533	<0.001
sex:dep_two	0.153	0.024	6.32	<0.001
age_ten:typet1dm	-0.196	0.109	-1.788	0.074
age_ten:typet2dm	-0.57	0.051	-11.209	<0.001
sex:typet1dm	0.999	0.327	3.058	0.002
sex:typet2dm	1.001	0.142	7.052	<0.001
dep_two:typet1dm	-0.399	0.189	-2.11	0.035
dep_two:typet2dm	-0.464	0.091	-5.093	<0.001
age_ten:sex:typet1dm	-0.312	0.081	-3.835	<0.001
age_ten:sex:typet2dm	-0.145	0.039	-3.747	<0.001
age_ten:dep_two:typet1dm	0.039	0.074	0.523	0.601

	Estimate	Std. Error	t value	Pr(>|t|)
age_ten:dep_two:typet2dm	0.138	0.035	3.949	<0.001
sex:dep_two:typet1dm	0.096	0.205	0.467	0.641
sex:dep_two:typet2dm	-0.241	0.073	-3.325	0.001

Logistic regression model with admission as the outcome. Age_ten is the age in years divided by ten and dep_two is the deprivation score divided by two.

Figure S4 Incidence rate of heart failure by diabetes type, deprivation and sex



The lines represent the predicted rates obtained from quasi-Poisson regression models of incident heart failure events on age, sex, deprivation and diabetes type, with interaction terms included where these improved model fit. Predictions were made for men and women aged 50.

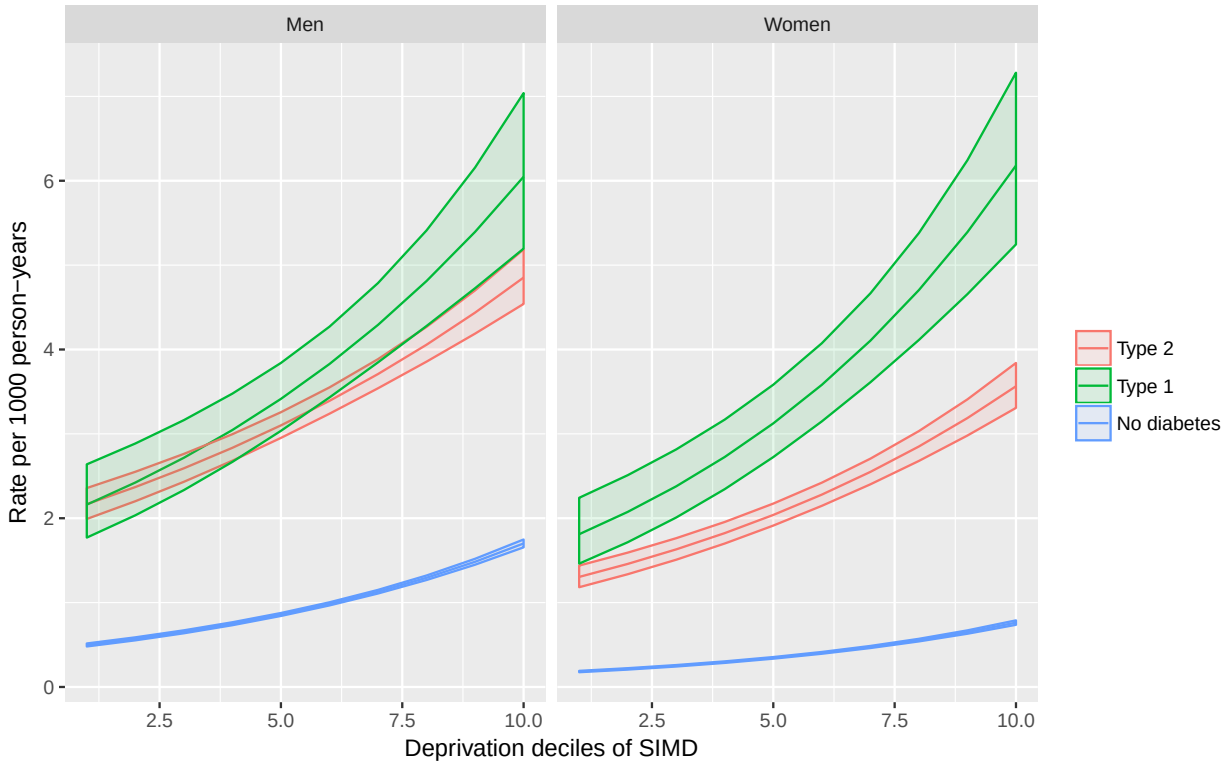
Table S8 Cross-sectional incidence rate model, coefficients and standard errors

	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-7.742	0.021	-372.393	<0.001
age_ten	1.131	0.007	154.279	<0.001
sex	-1.023	0.023	-45.447	<0.001
dep_two	0.683	0.014	47.613	<0.001
typet1dm	1.491	0.117	12.765	<0.001
typet2dm	1.518	0.053	28.734	<0.001
age_ten:sex	0.162	0.006	28.1	<0.001
age_ten:dep_two	-0.167	0.005	-32.915	<0.001

	Estimate	Std. Error	t value	Pr(>|t|)
sex:dep_two	0.11	0.012	9.364	<0.001
age_ten:typet1dm	-0.177	0.054	-3.294	0.001
age_ten:typet2dm	-0.289	0.02	-14.751	<0.001
sex:typet1dm	0.824	0.087	9.479	<0.001
sex:typet2dm	0.494	0.042	11.852	<0.001
dep_two:typet1dm	-0.111	0.079	-1.413	0.158
dep_two:typet2dm	-0.235	0.037	-6.433	<0.001
age_ten:sex:typet1dm	-0.204	0.041	-5.013	<0.001
age_ten:sex:typet2dm	-0.114	0.015	-7.363	<0.001
age_ten:dep_two:typet1dm	0.047	0.036	1.301	0.193
age_ten:dep_two:typet2dm	0.053	0.014	3.919	<0.001

Quasi-Poisson regression model with admissions or death as the outcome. Age_ten is the age in years divided by ten and dep_two is the deprivation score divided by two. The standard errors and P-values are scaled to allow for overdispersion.

Figure S5 Modelled rate of heart failure by diabetes type, deprivation and sex. Rates shown on absolute scale



This figure is is simiar to Figure one in the main manuscript, using the same regression model, but with deprivation rather than age being shown on the x-axis. The lines represent the predicted rates obtained from quasi-Poisson regression models of incident heart failure events on age, sex, deprivation and diabetes type, with interaction terms included where these improved model fit. Predictions were made at age 50.

Table S9 Time trends incidence rate model, coefficients and standard errors

	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-7.738	0.021	-373.826	<0.001
age_ten	1.135	0.007	155.51	<0.001
sex	-1.024	0.022	-45.789	<0.001
dep_two	0.682	0.014	47.877	<0.001
year	-0.009	0.003	-3.774	<0.001
typet1dm	1.511	0.116	13.031	<0.001
typet2dm	1.521	0.053	28.946	<0.001
age_ten:sex	0.161	0.006	28.112	<0.001
age_ten:dep_two	-0.168	0.005	-33.366	<0.001
sex:dep_two	0.111	0.012	9.485	<0.001
age_ten:year	-0.005	0.001	-5.481	<0.001
age_ten:typet1dm	-0.181	0.053	-3.399	0.001
age_ten:typet2dm	-0.287	0.02	-14.714	<0.001
sex:typet1dm	0.823	0.086	9.549	<0.001
sex:typet2dm	0.493	0.041	11.896	<0.001
dep_two:typet1dm	-0.116	0.078	-1.489	0.137
dep_two:typet2dm	-0.234	0.036	-6.453	<0.001
year:typet1dm	-0.022	0.01	-2.125	0.034
year:typet2dm	-0.004	0.003	-1.481	0.139
age_ten:sex:typet1dm	-0.206	0.04	-5.102	<0.001
age_ten:sex:typet2dm	-0.113	0.015	-7.399	<0.001
age_ten:dep_two:typet1dm	0.047	0.036	1.306	0.192
age_ten:dep_two:typet2dm	0.054	0.014	4.002	<0.001

Quasi-Poisson regression model with admissions or death as the outcome. Age_ten is the age in years divided by ten and dep_two is the deprivation score divided by two. The standard errors and P-values are scaled to allow for overdispersion.

Table S10 Estimates of non-parametric smooth functions

	Estimated degrees of freedom	Chi-squared	Approximate P-value
No diabetes	7.825	453.517	<0.001
Type 1	1.916	17.512	<0.001
Type 2	2.15	117.707	<0.001

Significance tests for the non-parametric smooth terms from a generalized additive model of incident heart failure events on age, sex, deprivation, diabetes type and calendar year, with interaction terms included where these improved model fit, using a log-link and Poisson likelihood, with correction of the standard errors for overdispersion. Penalized thin plate regression splines were used to model non-linear associations for calendar year by diagnosis type. Predictions were made for men and women aged 50.

Table S11, Heart failure case-fatality model, coefficients and standard errors

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-2.938	0.037	-79.507	<0.001
age_ten	0.239	0.024	10.07	<0.001
I(age_tenˆ2)	0.041	0.005	7.985	<0.001

	Estimate	Std. Error	z value	Pr(>|z|)
sex	0.041	0.02	2.077	0.038
dep_two	0.113	0.016	7.317	<0.001
typet1dm	0.649	0.104	6.248	<0.001
typet2dm	-0.046	0.031	-1.483	0.138
sex:typet1dm	-0.375	0.158	-2.377	0.017
sex:typet2dm	0.021	0.044	0.485	0.628

Logistic regression model with death as the outcome and admission or death as the denominator. Age_ten is the age in years divided by ten and dep_two is the deprivation score divided by two.

Table S12, Heart failure case-fatality over time model, coefficients and standard errors

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-2.917	0.037	-79.47	<0.001
age_ten	0.23	0.024	9.696	<0.001
I(age_ten^2)	0.044	0.005	8.521	<0.001
sex	0.036	0.018	2.064	0.039
dep_two	0.108	0.016	6.988	<0.001
year	-0.033	0.003	-10.135	<0.001
typet1dm	0.47	0.079	5.976	<0.001
typet2dm	-0.017	0.023	-0.768	0.442
year:typet1dm	0.01	0.027	0.38	0.704
year:typet2dm	-0.006	0.008	-0.817	0.414

Logistic regression model with death as the outcome and admission or death as the denominator. Age_ten is the age in years divided by ten and dep_two is the deprivation score divided by two.

Additional analysis - IHD admissions excluded

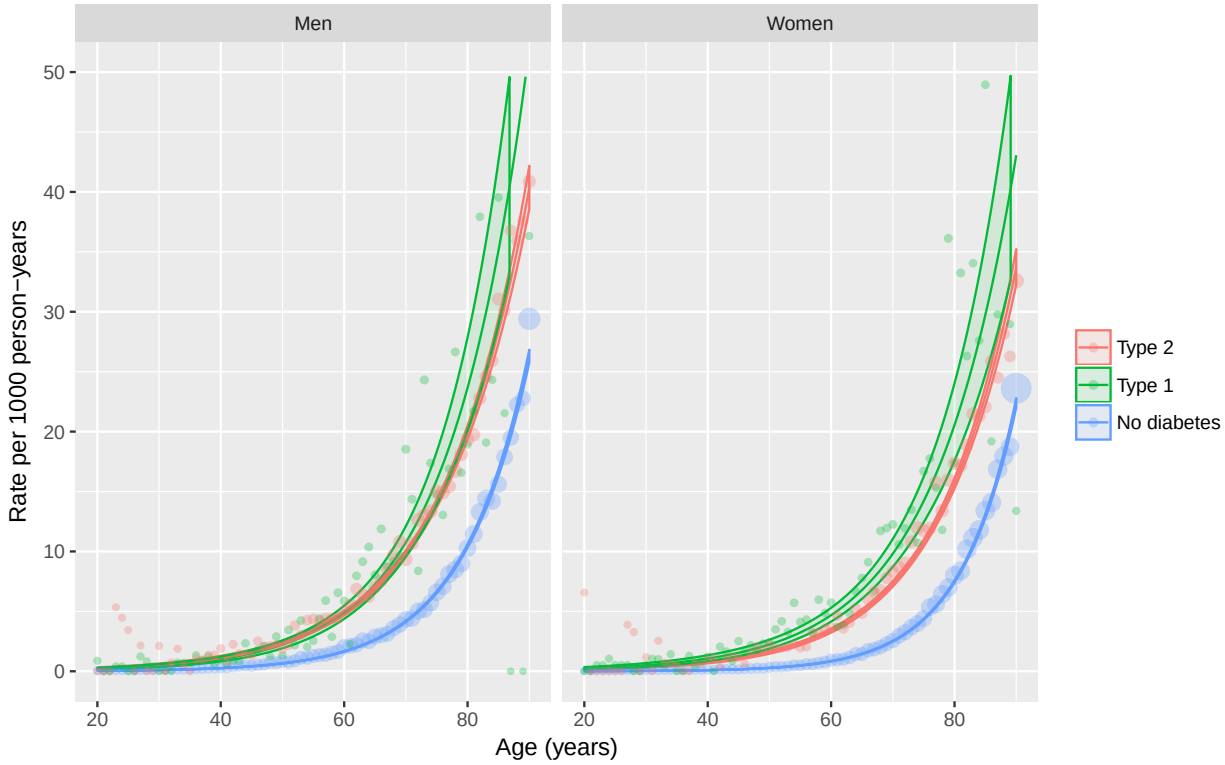
Table S13 Heart failure admissions and deaths by age, sex, deprivation and diagnosis with IHD admissions excluded

Age	Sex	Deprivation	Diagnosis	Admissions	Persontime
20 to 49	men	1-5	No diabetes	901	5069826
20 to 49	men	1-5	Type1	29	41407
20 to 49	men	1-5	Type 2	78	49272
20 to 49	men	6-10	No diabetes	1692	5263834
20 to 49	men	6-10	Type1	50	44543
20 to 49	men	6-10	Type 2	138	76831
20 to 49	women	1-5	No diabetes	397	5249540
20 to 49	women	1-5	Type1	diff	30878
20 to 49	women	1-5	Type 2	diff	31920
20 to 49	women	6-10	No diabetes	822	5601684
20 to 49	women	6-10	Type1	35	32785
20 to 49	women	6-10	Type 2	77	58653

Age	Sex	Deprivation	Diagnosis	Admissions	Persontime
50 to 59	men	1-5	No diabetes	1587	1693233
50 to 59	men	1-5	Type1	28	12659
50 to 59	men	1-5	Type 2	310	99493
50 to 59	men	6-10	No diabetes	2141	1458332
50 to 59	men	6-10	Type1	56	11988
50 to 59	men	6-10	Type 2	546	124173
50 to 59	women	1-5	No diabetes	588	1794491
50 to 59	women	1-5	Type1	24	8981
50 to 59	women	1-5	Type 2	117	57015
50 to 59	women	6-10	No diabetes	1123	1569973
50 to 59	women	6-10	Type1	47	8417
50 to 59	women	6-10	Type 2	246	87663
60 to 69	men	1-5	No diabetes	2834	1263927
60 to 69	men	1-5	Type1	50	7243
60 to 69	men	1-5	Type 2	871	145751
60 to 69	men	6-10	No diabetes	3678	1124789
60 to 69	men	6-10	Type1	63	6891
60 to 69	men	6-10	Type 2	1424	164762
60 to 69	women	1-5	No diabetes	1489	1411856
60 to 69	women	1-5	Type1	30	6061
60 to 69	women	1-5	Type 2	364	92946
60 to 69	women	6-10	No diabetes	2409	1287403
60 to 69	women	6-10	Type1	52	5749
60 to 69	women	6-10	Type 2	862	133206
70 to 79	men	1-5	No diabetes	3982	741231
70 to 79	men	1-5	Type1	45	3528
70 to 79	men	1-5	Type 2	1559	122825
70 to 79	men	6-10	No diabetes	4860	704115
70 to 79	men	6-10	Type1	72	3448
70 to 79	men	6-10	Type 2	1962	136811
70 to 79	women	1-5	No diabetes	3334	943974
70 to 79	women	1-5	Type1	49	3833
70 to 79	women	1-5	Type 2	1042	104267
70 to 79	women	6-10	No diabetes	5120	987247
70 to 79	women	6-10	Type1	67	4025
70 to 79	women	6-10	Type 2	1833	143606
80 to 89	men	1-5	No diabetes	5219	340043
80 to 89	men	1-5	Type1	19	929
80 to 89	men	1-5	Type 2	1284	50231
80 to 89	men	6-10	No diabetes	5336	314982
80 to 89	men	6-10	Type1	26	856
80 to 89	men	6-10	Type 2	1284	47422
80 to 89	women	1-5	No diabetes	8582	642195
80 to 89	women	1-5	Type1	28	1271
80 to 89	women	1-5	Type 2	1412	65181
80 to 89	women	6-10	No diabetes	9563	654989
80 to 89	women	6-10	Type1	46	1353
80 to 89	women	6-10	Type 2	1739	75363

Numbers less than or equal to 5, or where the difference from Table S1 is less than or equal to 5 were suppressed to maintain confidentiality.

Figure S6 Modelled rate of heart failure by diabetes type, age and sex with IHD admissions excluded



The lines represent the predicted rates obtained from quasi-Poisson regression models of incident heart failure events on age, sex, deprivation and diabetes type, with interaction terms included where these improved model fit. Predictions were made at the median deprivation score. Points represent event rates stratified by age (in years), sex and diabetes type.

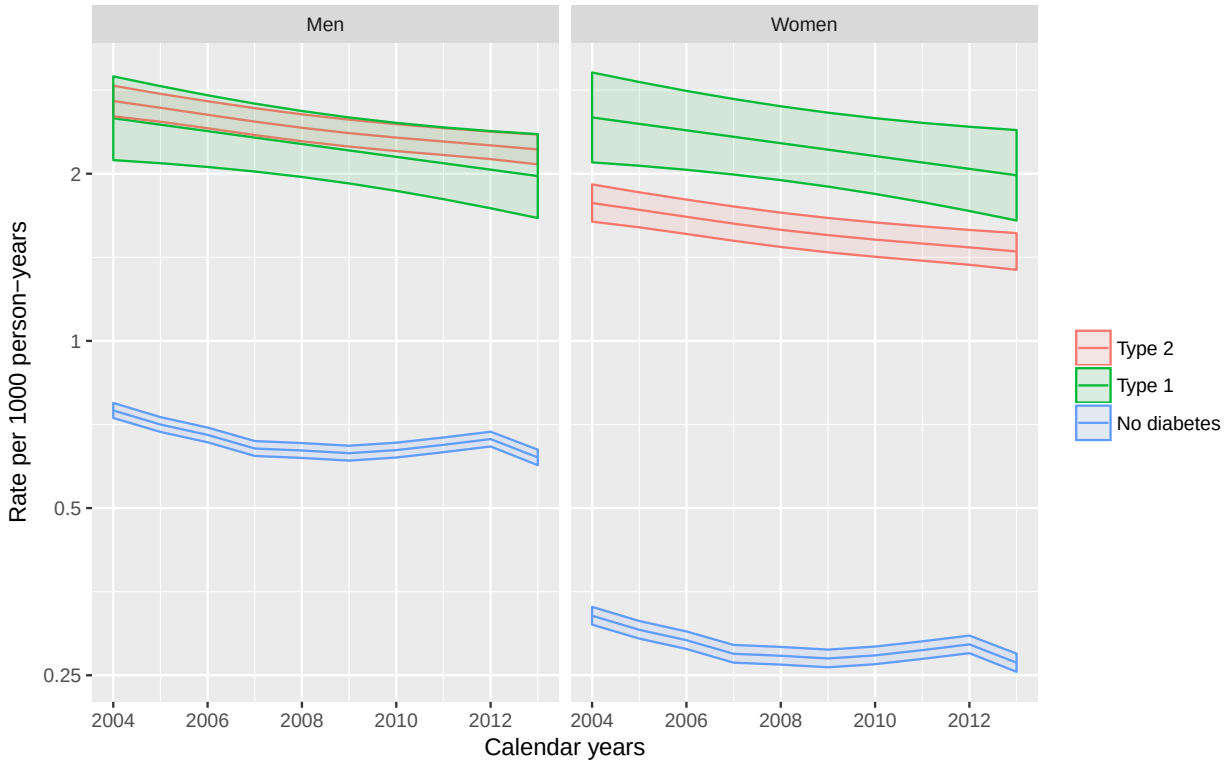
Table S14 Cross-sectional model, coefficients and standard errors with IHD admissions excluded

	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-7.945	0.024	-326.852	<0.001
age_ten	1.079	0.009	124.583	<0.001
sex	-0.956	0.027	-36.019	<0.001
dep_two	0.621	0.017	36.802	<0.001
typet1dm	1.329	0.144	9.237	<0.001
typet2dm	1.481	0.062	23.86	<0.001
age_ten:sex	0.173	0.007	25.265	<0.001
age_ten:dep_two	-0.158	0.006	-26.279	<0.001
sex:dep_two	0.105	0.014	7.368	<0.001
age_ten:typet1dm	-0.222	0.068	-3.254	0.001
age_ten:typet2dm	-0.261	0.023	-11.256	<0.001
sex:typet1dm	0.855	0.108	7.927	<0.001
sex:typet2dm	0.43	0.049	8.763	<0.001
dep_two:typet1dm	-0.113	0.098	-1.161	0.246
dep_two:typet2dm	-0.187	0.043	-4.361	<0.001

	Estimate	Std. Error	t value	Pr(>|t|)
age_ten:sex:typet1dm	-0.221	0.052	-4.29	<0.001
age_ten:sex:typet2dm	-0.112	0.018	-6.158	<0.001
age_ten:dep_two:typet1dm	0.089	0.046	1.928	0.054
age_ten:dep_two:typet2dm	0.044	0.016	2.753	0.006

Quasi-Poisson regression model with admissions or death as the outcome. Age_ten is the age in years divided by ten and dep_two is the deprivation score divided by two. The standard errors and P-values are scaled to allow for overdispersion.

Figure S7 Trends in rates of heart failure by diabetes type, sex and calendar year with IHD admissions excluded



The lines represent the predicted rates obtained from generalized additive models of incident heart failure events on age, sex, deprivation, diabetes type and calendar year, with interaction terms included where these improved model fit, using a log-link and Poisson likelihood, with correction of the standard errors for overdispersion. Penalized thin plate regression splines were used to model non-linear associations for calendar year by diagnosis type. Predictions were made for men and women aged 50.

Table S15 Time trends model, coefficients and standard errors with IHD admissions excluded

	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-7.941	0.024	-327.026	<0.001

	Estimate	Std. Error	t value	Pr(>|t|)
age_ten	1.082	0.009	125.008	<0.001
sex	-0.957	0.026	-36.164	<0.001
dep_two	0.621	0.017	36.892	<0.001
year	-0.006	0.003	-2.127	0.033
typet1dm	1.343	0.144	9.36	<0.001
typet2dm	1.486	0.062	23.988	<0.001
age_ten:sex	0.172	0.007	25.252	<0.001
age_ten:dep_two	-0.158	0.006	-26.502	<0.001
sex:dep_two	0.105	0.014	7.426	<0.001
age_ten:year	-0.003	0.001	-3.302	0.001
age_ten:typet1dm	-0.224	0.068	-3.301	0.001
age_ten:typet2dm	-0.258	0.023	-11.183	<0.001
sex:typet1dm	0.854	0.107	7.955	<0.001
sex:typet2dm	0.428	0.049	8.763	<0.001
dep_two:typet1dm	-0.117	0.097	-1.197	0.231
dep_two:typet2dm	-0.187	0.043	-4.36	<0.001
year:typet1dm	-0.015	0.013	-1.15	0.25
year:typet2dm	-0.007	0.003	-2.2	0.028
age_ten:sex:typet1dm	-0.222	0.051	-4.335	<0.001
age_ten:sex:typet2dm	-0.112	0.018	-6.176	<0.001
age_ten:dep_two:typet1dm	0.089	0.046	1.932	0.053
age_ten:dep_two:typet2dm	0.045	0.016	2.79	0.005

Quasi-Poisson regression model with admissions or death as the outcome. Age_ten is the age in years divided by ten and dep_two is the deprivation score divided by two. The standard errors and P-values are scaled to allow for overdispersion.

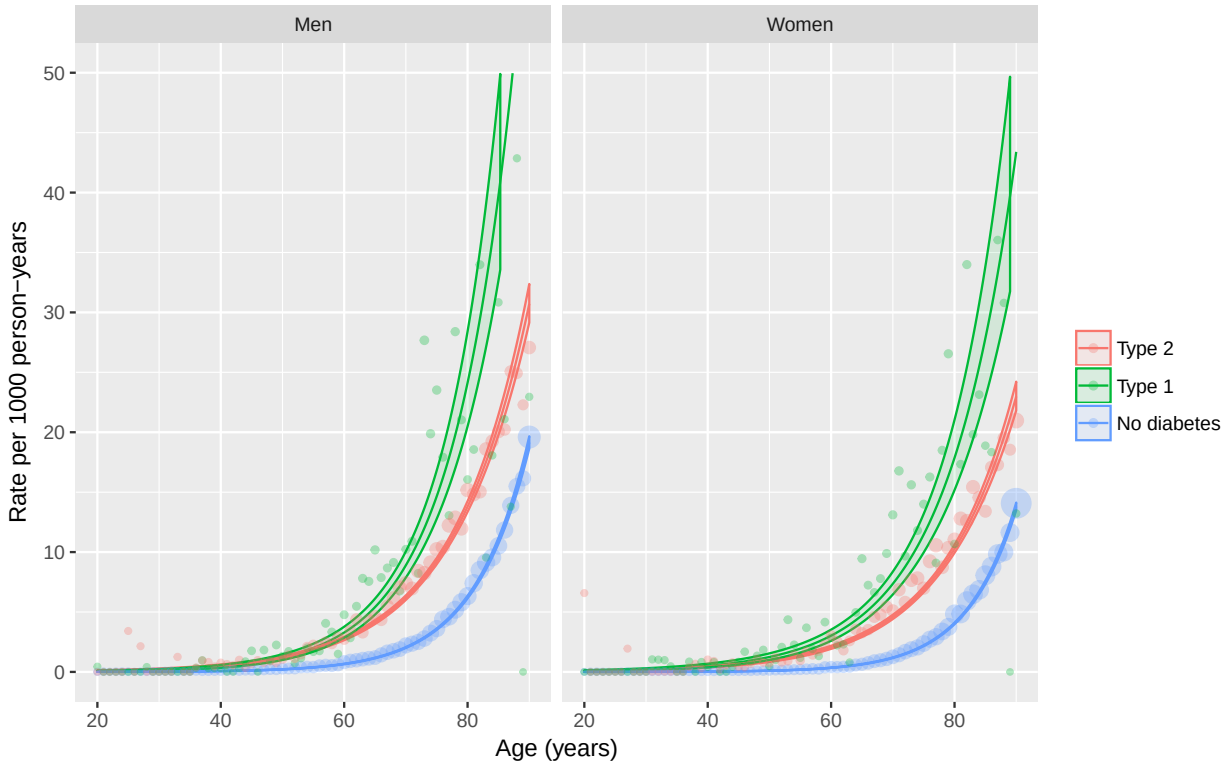
Table S16 Estimates of non-parametric smooth functions with IHD admissions excluded

	Estimated degrees of freedom	Chi-squared	Approximate P-value
No diabetes	7.646	214.152	<0.001
Type 1	1.005	4.75	0.03
Type 2	1.968	66.125	<0.001

Significance tests for the non-parametric smooth terms from a generalized additive model of incident heart failure events on age, sex, deprivation, diabetes type and calendar year, with interaction terms included where these improved model fit, using a log-link and Poisson likelihood, with correction of the standard errors for overdispersion. Penalized thin plate regression splines were used to model non-linear associations for calendar year by diagnosis type.

Sensitivity analysis - Events coded in First position only

Figure S8 Modelled rate of heart failure by diabetes type, age and sex with diagnosis recored in first position only



The lines represent the predicted rates obtained from quasi-Poisson regression models of incident heart failure events on age, sex, deprivation and diabetes type, with interaction terms included where these improved model fit. Predictions were made at the median deprivation score. Points represent event rates stratified by age (in years), sex and diabetes type.

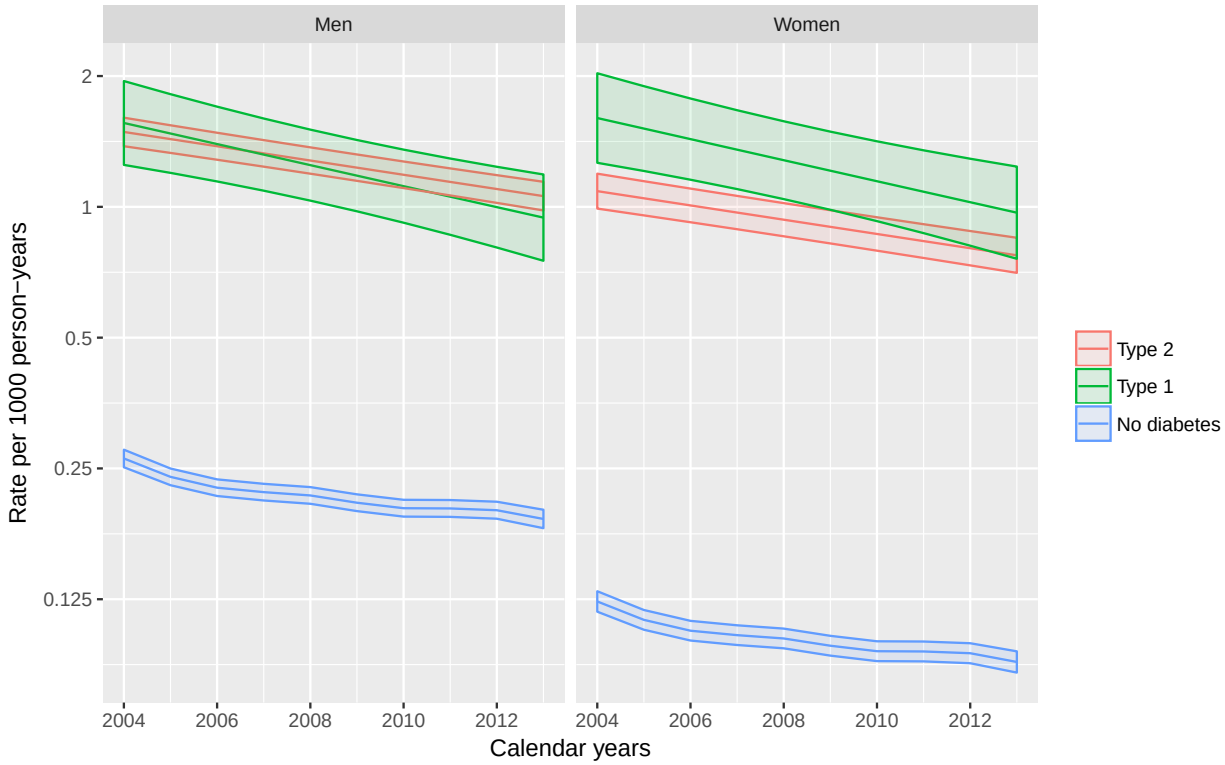
Table S17 Cross-sectional model, coefficients and standard errors with diagnosis recored in first position only

	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-9.264	0.039	-236.959	<0.001
age_ten	1.319	0.013	100.519	<0.001
sex	-0.864	0.038	-22.468	<0.001
dep_two	0.828	0.026	31.31	<0.001
typet1dm	1.839	0.196	9.38	<0.001
typet2dm	2.031	0.082	24.651	<0.001
age_ten:sex	0.108	0.01	10.731	<0.001
age_ten:dep_two	-0.199	0.009	-22.317	<0.001
sex:dep_two	0.107	0.018	5.809	<0.001
age_ten:typet1dm	-0.173	0.083	-2.078	0.038
age_ten:typet2dm	-0.403	0.03	-13.568	<0.001
sex:typet1dm	0.785	0.14	5.613	<0.001
sex:typet2dm	0.446	0.063	7.124	<0.001

	Estimate	Std. Error	t value	Pr(>|t|)
dep_two:typet1dm	-0.119	0.13	-0.916	0.359
dep_two:typet2dm	-0.28	0.056	-4.996	<0.001
age_ten:sex:typet1dm	-0.217	0.061	-3.537	<0.001
age_ten:sex:typet2dm	-0.102	0.023	-4.51	<0.001
age_ten:dep_two:typet1dm	0.05	0.056	0.902	0.367
age_ten:dep_two:typet2dm	0.083	0.02	4.095	<0.001

Quasi-Poisson regression model with admissions or death as the outcome. Age_ten is the age in years divided by ten and dep_two is the deprivation score divided by two. The standard errors and P-values are scaled to allow for overdispersion.

Figure S9 Trends in rates of heart failure by diabetes type, sex and calendar year with with diagnosis recored in first position only



The lines represent the predicted rates obtained from generalized additive models of incident heart failure events on age, sex, deprivation, diabetes type and calendar year, with interaction terms included where these improved model fit, using a log-link and Poisson likelihood, with correction of the standard errors for overdispersion. Penalized thin plate regression splines were used to model non-linear associations for calendar year by diagnosis type. Predictions were made for men and women aged 50.

Table S18 Time trends model, coefficients and standard errors with diagnosis recored in first position only

	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-9.25	0.039	-237.045	<0.001
age_ten	1.322	0.013	100.86	<0.001
sex	-0.865	0.038	-22.57	<0.001
dep_two	0.826	0.026	31.325	<0.001
year	-0.03	0.004	-6.762	<0.001
typet1dm	1.863	0.195	9.548	<0.001
typet2dm	2.04	0.082	24.809	<0.001
age_ten:sex	0.107	0.01	10.652	<0.001
age_ten:dep_two	-0.2	0.009	-22.51	<0.001
sex:dep_two	0.108	0.018	5.877	<0.001
age_ten:year	0	0.002	-0.052	0.958
age_ten:typet1dm	-0.178	0.083	-2.152	0.031
age_ten:typet2dm	-0.401	0.03	-13.517	<0.001
sex:typet1dm	0.784	0.139	5.629	<0.001
sex:typet2dm	0.444	0.063	7.102	<0.001
dep_two:typet1dm	-0.125	0.129	-0.971	0.331
dep_two:typet2dm	-0.279	0.056	-4.974	<0.001
year:typet1dm	-0.025	0.015	-1.683	0.092
year:typet2dm	-0.007	0.004	-1.781	0.075
age_ten:sex:typet1dm	-0.219	0.061	-3.588	<0.001
age_ten:sex:typet2dm	-0.102	0.023	-4.512	<0.001
age_ten:dep_two:typet1dm	0.05	0.055	0.906	0.365
age_ten:dep_two:typet2dm	0.084	0.02	4.135	<0.001

Quasi-Poisson regression model with admissions or death as the outcome. Age_ten is the age in years divided by ten and dep_two is the deprivation score divided by two. The standard errors and P-values are scaled to allow for overdispersion.

Table S19 Estimates of non-parametric smooth functions with with diagnosis recored in first position only

	Estimated degrees of freedom	Chi-squared	Approximate P-value
No diabetes	5.772	294.872	<0.001
Type 1	1.01	15.662	<0.001
Type 2	1.018	127.99	<0.001

Significance tests for the non-parametric smooth terms from a generalized additive model of incident heart failure events on age, sex, deprivation, diabetes type and calendar year, with interaction terms included where these improved model fit, using a log-link and Poisson likelihood, with correction of the standard errors for overdispersion. Penalized thin plate regression splines were used to model non-linear associations for calendar year by diagnosis type.

Legend for interactive figure

The interactive figure is available at https://ihwph-hehta.shinyapps.io/dm_hf_fig2/.

This figure is an interactive version of Figure 2 which can be found in the main manuscript. The lines represent the predicted rates obtained from generalized additive models of incident heart failure events. The

ribbons are 95% confidence intervals. Covariates included in the model were age, sex, deprivation, diabetes type and calendar-year, with interaction terms included where these improved model fit. The model was fit with a log-link and Poisson likelihood, with correction of the standard errors for overdispersion. Penalized thin plate regression splines were used to model non-linear associations for calendar-year by diagnosis type.

References

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2. Barnard, J. and Rubin, D.B. Small sample degrees of freedom with multiple imputation. Biometrika. 1999;86:948-955.